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=> dis his

     (FILE 'HOME' ENTERED AT 09:36:34 ON 05 APR 2002)

     FILE 'MEDLINE, CAPLUS, EMBASE' ENTERED AT 09:36:54 ON 05 APR 2002
L1             7 S FCGAMMAR1
L2            65 S FC (1N) GAMMA (1N) R1
L3          1957 S FC (1N) GAMMA (1N) RI
L4           982 S CD64
L5             0 S L1 AND L2 AND L3 AND L4
L6          2547 S L1 OR L2 OR L3 OR L4
L7          1130 S L6 (P) ANTIBOD?
L8            54 S L7 (P) ADMINIST?
L9            26 DUP REM L8 (28 DUPLICATES REMOVED)
L10          585 S VAN DE WINKEL?/AU
L11         1074 S L10 AND MACROPHAGE? OR CD64
L12          183 S L10 AND (MACROPHAGE? OR CD64)
L13          127 S L12 (P) ANTIBOD?
L14           11 S L13 (P) ADMINIST?
L15            7 DUP REM L14 (4 DUPLICATES REMOVED)
L16          299 S L4 (P) MACROPHAGE?
L17            0 S L16 AND PSORIASIS
L18           10 S L16 AND (HIV)
L19            5 DUP REM L18 (5 DUPLICATES REMOVED)
L20           23 S L16 AND (LUPUS OR SCLERODERMA OR DERMATITIS OR WEGENER? OR RA
L21           12 DUP REM L20 (11 DUPLICATES REMOVED)
L22          816 S (MAB (1N) 22) OR H22 OR (CRL (1N) 1117)
L23           58 S L22 (P) ADMINIST?
L24           35 DUP REM L23 (23 DUPLICATES REMOVED)
L25           33 S L24  NOT L7
L26          458 S CL2MDP
L27           10 S L26 (10N) ANTIBOD?
L28            5 DUP REM L27 (5 DUPLICATES REMOVED)

=> end
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09/401,896

9941285

WEST Search History

DATE: Friday, April 05, 2002

Set Name side by side	Query	Hit Count	Set Name result set
	DB=DWPI; PLUR=YES; OP=OR		
L14	cl2mdp	1	L14
L13	(9941285)[PN]	2	L13
L12	9941285	2	L12
	DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=OR		
L11	L9 same (contact or administ$6)	1	L11
L10	L9 near (contact or administ$6)	0	L10
L9	L8 near antibod$4	16	L9
L8	cd64 or (fcgammaR1) or (fc adj gamma adj R1) or (fc adj gamma adj FCRI) or (fc adj gamma adj receptor$4)	316	L8
L7	cd64 or (fcgammaR1) or (fc adj gamma adj R1) or (fc adj gamma adj FCRI)	189	L7
L6	L5 and macrophage$4	4	L6
L5	(van adj de adj winkel)[IN]	9	L5
L4	L2 and (cd64 or cd32 or cd16)	18	L4
L3	L2 and cd64	3	L3
L2	L1 and macrophage?	303	L2
L1	(van de winkel)[IN]	115578	L1

END OF SEARCH HISTORY

WEST

Generate Collection | Print

Search Results - Record(s) 1 through 10 of 16 returned.

1. Document ID: US 20010038843 A1

L9: Entry 1 of 16 File: PGPB Nov 8, 2001

DOCUMENT-IDENTIFIER: US 20010038843 A1
TITLE: ENHANCED VACCINES

Detail Description Paragraph (37):
[0066] The vaccines, vaccine conjugates, and immunogenic polypeptides described herein can be administered alone or in combination with other components. For example, a vaccine conjugate can contain a blocking molecule that inhibits the interaction between an antibody (e.g., an IgG antibody) and an Fc-gamma receptor II (e.g., CD32). Such blocking molecules (i.e., Fc-gamma receptor II blocking molecules) can include, without limitation, anti-CD32 antibodies. Anti-CD32 antibodies can be obtained using common antibody production and screening techniques. It is noted that Fc-gamma receptor II blocking molecules can be used in combination with any immunogenic polypeptide such that the immune response against the immunogenic polypeptide is enhanced. For example, a mixture containing an anti-CD32 antibody and an immunogenic polypeptide either conjugated or not can be administered to a mammal to induce a potent immune response against the immunogenic polypeptide.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw Desc
Image

2. Document ID: US 20010001310 A1

L9: Entry 2 of 16 File: PGPB May 17, 2001

DOCUMENT-IDENTIFIER: US 20010001310 A1
TITLE: Bispecific antibodies for retargeting anticancer cytotoxic lymphocytes

Detail Description Paragraph (12):
41. Other methods can be utilized in producing bispecific antibodies. Chemical heteroconjugates can be created by the chemical linking of either intact antibodies or antibody fragments of different specificities. Karpovsky et al., Production of Target-Specific Effector Cells Using Hetero-Cross-Linked Aggregates Containing Anti-Target Cell and Anti-Fc Gamma Receptor Antibodies, J. Exp. Med. 160: 1686-1701 (1984). However, these heteroconjugates are difficult to make in a reproducible manner and are at least twice as large as normal monoclonal antibodies. Bispecific antibodies may also be created by disulfide exchange, which involves enzymatic cleavage and reassociation of the antibody fragments. Glennie et al., Preparation and Performance of Bispecific F(ab').sub.2 Antibody Containing Thioether Linked Fab' Fragments, J. Immunol. 139: 2367-2375 (1987). Another method is the creation of F(ab').sub.2 connected via a shortened Fc to the leucine zipper region of the transcription factors Fos and Jun. Kostelny et al., Formation of a Bispecific Monoclonal Antibody by the Use of Leucine Zippers, J. Immunol. 148: 1547-53 (1992).

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw Desc
Image

3. Document ID: US 6300478 B1

L9: Entry 3 of 16 File: USPT Oct 9, 2001

DOCUMENT-IDENTIFIER: US 6300478 B1
TITLE: Antibodies to natural killer stimulatory factor

Brief Summary Paragraph Right (1):
Natural killer (NK) cells are a subset of lymphocytes active in the immune system and representing an average 15% of mononuclear cells in human peripheral blood [G. Trinchieri and B. Perussia, Lab. Invest., 50:489 (1984)]. Among the surface markers used to identify human NK cells is a receptor binding with low affinity to the Fc fragment of IgG antibodies, such as Fc-gamma receptor III or CD16 antigen [B. Perussia et al, J. Immunol., 133:180 (1984)]. NK cells have been demonstrated to play an important role in vivo in the defense against tumors, tumor metastases, virus infection, and to regulate normal and malignant hematopoiesis.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw Desc
Image

4. Document ID: US 6207805 B1

L9: Entry 4 of 16 File: USPT Mar 27, 2001

DOCUMENT-IDENTIFIER: US 6207805 B1
TITLE: Prostate cell surface antigen-specific antibodies

Detailed Description Paragraph Right (12):
Other methods can be utilized in producing bispecific antibodies. Chemical heteroconjugates can be created by the chemical linking of either intact antibodies or antibody fragments of different specificities. Karpovsky et al., Production of Target-Specific Effector Cells Using Hetero-Cross-Linked Aggregates Containing Anti-Target Cell and Anti-Fc Gamma Receptor Antibodies, J. Exp. Med. 160: 1686-1701 (1984). However, these heteroconjugates are difficult to make in a reproducible manner and are at least twice as large as normal monoclonal antibodies. Bispecific antibodies may also be created by disulfide exchange, which involves enzymatic cleavage and reassociation of the antibody fragments. Glennie et al., Preparation and Performance of Bispecific F(ab').sub.2 Antibody Containing Thioether Linked Fab' Fragments, J. Immunol. 139: 2367-2375 (1987). Another method is the creation of F(ab').sub.2 connected via a shortened Fc to the leucine zipper region of the transcription factors Fos and Jun. Kostelny et al., Formation of a Bispecific Monoclonal Antibody by the Use of Leucine Zippers, J. Immunol. 148: 1547-53 (1992).

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWMC | Draw Desc
Image

5. Document ID: US 6146837 A

L9: Entry 5 of 16 File: USPT Nov 14, 2000

DOCUMENT-IDENTIFIER: US 6146837 A
TITLE: Cyanidin compositions and therapeutic and diagnostic uses therefor

Detailed Description Paragraph Right (60):
PE-Cy5 staining of Fc.gamma.RI-expressing cells was blocked to an extent greater than 90%, by treating cells with either 20% human pooled serum, or with a monoclonal CD64 antibody blocking the Fc.gamma.RI-ligand-binding region (mAb 197, Van de Winkel J G J, et al., 1993, Immunol Today 14:215), or with aggregated IgG. Exemplary data (FIG. 1e) show PE-Cy5 conjugate staining of monocytes reduced by greater than 80% in whole blood staining assays.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

6. Document ID: US 5811523 A

L9: Entry 6 of 16 File: USPT Sep 22, 1998

DOCUMENT-IDENTIFIER: US 5811523 A
TITLE: Antibodies to natural killer stimulatory factor

Brief Summary Paragraph Right (2):
Natural killer (NK) cells are a subset of lymphocytes active in the immune system and representing an average 15% of mononuclear cells in human peripheral blood [G. Trinchieri and B. Perussia, Lab. Invest., 50:489 (1984)]. Among the surface markers used to identify human NK cells is a receptor binding with low affinity to the Fc fragment of IgG antibodies, such as Fc-gamma receptor III or CD16 antigen [B. Perussia et al, J. Immunol., 133:180 (1984)]. NK cells have been demonstrated to play an important role in vivo in the defense against tumors, tumor metastases, virus infection, and to regulate normal and malignant hematopoiesis.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

7. Document ID: US 5648467 A

L9: Entry 7 of 16 File: USPT Jul 15, 1997

DOCUMENT-IDENTIFIER: US 5648467 A
TITLE: Natural killer cell stimulatory factor

Brief Summary Paragraph Right (2):
Natural killer (NK) cells are a subset of lymphocytes active in the immune system and representing an average 15% of mononuclear cells in human peripheral blood [G.

Trinchieri and B. Perussia, Lab. Invest., 50:489 (1984)]. Among the surface markers used to identify human NK cells is a receptor binding with low affinity to the Fc fragment of IgG antibodies, such as Fc-gamma receptor III or CD16 antigen [B. Perussia et al, J. Immunol., 133:180 (1984)]. NK cells have been demonstrated to play an important role in vivo in the defense against tumors, tumor metastases, virus infection, and to regulate normal and malignant hematopoiesis.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWMC | Draw Desc | Image

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8. Document ID: US 5648072 A

L9: Entry 8 of 16 File: USPT Jul 15, 1997

DOCUMENT-IDENTIFIER: US 5648072 A
TITLE: Methods of inducing gamma interferon and stimulating blood cell populations using natural killer stimulatory factor

Brief Summary Paragraph Right (2):
Natural killer (NK) cells are a subset of lymphocytes active in the immune system and representing an average 15% of mononuclear cells in human peripheral blood [G. Trinchieri and B. Perussia, Lab. Invest., 50:489 (1984)]. Among the surface markers used to identify human NK cells is a receptor binding with low affinity to the Fc fragment of IgG antibodies, such as Fc-gamma receptor III or CD16 antigen [B. Perussia et al, J. Immunol., 133:180 (1984)]. NK cells have been demonstrated to play an important role in vivo in the defense against tumors, tumor metastases, virus infection, and to regulate normal and malignant hematopoiesis.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWMC | Draw Desc | Image

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9. Document ID: US 5569454 A

L9: Entry 9 of 16 File: USPT Oct 29, 1996

DOCUMENT-IDENTIFIER: US 5569454 A
TITLE: Methods of treating infection using natural killer stimulatory factor

Brief Summary Paragraph Right (2):
Natural killer (NK) cells are a subset of lymphocytes active in the immune system and representing an average 15% of mononuclear cells in human peripheral blood [G. Trinchieri and B. Perussia, Lab. Invest., 50:489 (1984)]. Among the surface markers used to identify human NK cells is a receptor binding with low affinity to the Fc fragment of-IgG antibodies, such as Fc-gamma receptor III or CD16 antigen [B. Perussia et al, J. Immunol., 133:180 (1984)]. NK cells have been demonstrated to play an important role in vivo in the defense against tumors, tumor metastases, virus infection, and to regulate normal and malignant hematopoiesis.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWMC | Draw Desc | Image

10. Document ID: US 5457038 A

L9: Entry 10 of 16 File: USPT Oct 10, 1995

DOCUMENT-IDENTIFIER: US 5457038 A
TITLE: Natural killer stimulatory factor

Brief Summary Paragraph Right (1):
Natural killer (NK) cells are a subset of lymphocytes active in the immune system and representing an average 15% of mononuclear cells in human peripheral blood [G. Trinchieri and B. Perussia, Lab. Invest., 5.0:489 (1984)]. Among the surface markers used to identify human NK cells is a receptor binding with low affinity to the Fc fragment of IgG antibodies, such as Fc-gamma receptor III or CD16 antigen [B. Perussia et al, J. Immunol., 133:180 (1984)]. NK cells have been demonstrated to play an important role in vivo in the defense against tumors, tumor metastases, virus infection, and to regulate normal and malignant hematopoiesis.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Image | KWIC | Draw Desc

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L8 near antibod$4	16

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Search Results - Record(s) 11 through 16 of 16 returned.

11. Document ID: EP 739904 A1

L9: Entry 11 of 16 File: EPAB Oct 30, 1996

DOCUMENT-IDENTIFIER: EP 739904 A1
TITLE: Bispecific reagents for aids therapy

Abstract (1):
Bispecific molecules which react both with the high-affinity Fc gamma receptor of human effector cells and with a virus or virus component are disclosed. Binding of the molecules to the Fc receptors found on effector cells is not blocked by human immunoglobulin G. The molecules are useful for targeting human effector cells (e.g. macrophages) against a viral target (e.g. HIV or BIV-infected cell). For this purpose, bispecific molecules can be constructed containing the binding region derived from an anti-Fc gamma receptor antibody and the CD4 molecule or CD4 binding domain of the envelope glycoprotein gp120 of BIV. Alternatively, bispecific antibodies or heteroantibodies can be constructed containing the binding region derived from an anti-Fc receptor antibody and the binding region of HIV-specific antibody such as anti-gp120 antibody. Targeted effector cells can be used to kill virus by cell mediated antibody dependent cytolysis.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

12. Document ID: WO 9105871 A1

L9: Entry 12 of 16 File: EPAB May 2, 1991

DOCUMENT-IDENTIFIER: WO 9105871 A1
TITLE: BISPECIFIC HETEROANTIBODIES WITH DUAL EFFECTOR FUNCTIONS

Abstract (1):
CHG DATE=19990617 STATUS=O>Bispecific molecules which react both with the high-affinity Fc gamma receptor of human effector cells and with a target cell surface antigen are disclosed. Binding of the molecules to the Fc receptors found on effector cells is not blocked by human immunoglobulin G. The molecules are useful for targeting human effector cells (e.g. macrophages) against cells bearing the target antigen. For this purpose, bispecific molecules can be constructed containing the binding region derived from an anti-Fc gamma receptor antibody and the binding region derived from an antibody specific for the target antigen. Targeted effector cells can be used to destroy cells bearing the target cell surface antigen by cell-mediated antibody dependent cytolysis and by complement-fixation.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc
Image

13. Document ID: WO 9100360 A1

L9: Entry 13 of 16 File: EPAB Jan 10, 1991

DOCUMENT-IDENTIFIER: WO 9100360 A1
TITLE: BISPECIFIC REAGENTS FOR AIDS THERAPY

Abstract (1):
Bispecific molecules which react both with the high-affinity Fc gamma receptor of human effector cells and with a virus or virus component are disclosed. Binding of the molecules to the Fc receptors found on effector cells is not blocked by human immunoglobulin G. The molecules are useful for targeting human effector cells (e.g. macrophages) against a viral target (e.g. HIV or HIV-infected cell). For this purpose, bispecific molecules can be constructed containing the binding region derived from an anti-Fc gamma receptor antibody and the CD4 molecule or CD4 binding domain of the envelope glycoprotein gp120 of HIV. Alternatively, bispecific antibodies or heteroantibodies can be constructed containing the binding region derived from an anti-Fc receptor antibody and the binding region of a HIV-specific antibody such as anti-gp120 antibody. Targeted effector cells can be used to kill virus by cell mediated antibody dependent cytolysis.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc
Image

14. Document ID: WO 200202801 A1

L9: Entry 14 of 16 File: DWPI Jan 10, 2002

DERWENT-ACC-NO: 2002-154755
DERWENT-WEEK: 200220

TITLE: Assaying function of Fc fragment in antibody, particularly in determining antibody-dependent cell-mediated cytotoxicity of antibody drugs with anti-cancer and antiviral action, e.g. in quality control

Basic Abstract Text:
DESCRIPTION OF DRAWING(S) - The drawing shows the results of flow-cytometric detection of mouse anti-human CD16 antibody and mouse anti-human CD64 antibody with expressed Fc gamma -RI (CD64) and Fc gamma RIII (CD16), respectively, on cells of THP-1 cell line. (Drawing includes non-English language text).

Basic Abstract Text (7):
DESCRIPTION OF DRAWING(S) - The drawing shows the results of flow-cytometric detection of mouse anti-human CD16 antibody and mouse anti-human CD64 antibody with expressed Fc gamma -RI (CD64) and Fc gamma RIII (CD16), respectively, on cells of THP-1 cell line. (Drawing includes non-English language text).

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Image | KWIC | Draw Desc

15. Document ID: DE 19905012 A1, EP 1025855 A1

L9: Entry 15 of 16 File: DWPI Aug 10, 2000

DERWENT-ACC-NO: 2000-492297
DERWENT-WEEK: 200045

TITLE: Composition comprising two antibodies, useful for immunotherapy of autoimmune disease, one directed against T-cell receptor, the other against Fc gamma receptor

Basic Abstract Text:
NOVELTY - Composition or mixture (A) containing at least one anti-T-cell receptor CD3 antibody (Ab1) and at least one anti-Fc gamma receptor antibody (Ab2).

Basic Abstract Text (1):
NOVELTY - Composition or mixture (A) containing at least one anti-T-cell receptor CD3 antibody (Ab1) and at least one anti-Fc gamma receptor antibody (Ab2).

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Image | KWIC | Draw Desc

16. Document ID: US 2001055592 A1, DE 19723690 A1, WO 9929731 A1, EP 951481 A1, US 2001009898 A1, JP 2001511821 W

L9: Entry 16 of 16 File: DWPI Dec 27, 2001

DERWENT-ACC-NO: 1998-194737
DERWENT-WEEK: 200206

TITLE: Use of Fc-gamma receptor antibodies - for treating amyotrophic lateral sclerosis

Standard Title Terms:
FC GAMMA RECEPTOR ANTIBODY TREAT AMYOTROPHIC LATERAL SCLEROSIS

Title (1):
Use of Fc-gamma receptor antibodies - for treating amyotrophic lateral sclerosis

Standard Title Terms (1):
FC GAMMA RECEPTOR ANTIBODY TREAT AMYOTROPHIC LATERAL SCLEROSIS

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Image | KWIC | Draw Desc

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Search Results - Record(s) 1 through 10 of 16 returned.

1. Document ID: US 20010038843 A1

L9: Entry 1 of 16 File: PGPB Nov 8, 2001

PGPUB-DOCUMENT-NUMBER: 20010038843
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20010038843 A1

TITLE: ENHANCED VACCINES

PUBLICATION-DATE: November 8, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
HELLMAN, LARS T.	UPPSALA		SE	

US-CL-CURRENT: 424/185.1; 424/192.1, 530/387.3

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

2. Document ID: US 20010001310 A1

L9: Entry 2 of 16 File: PGPB May 17, 2001

PGPUB-DOCUMENT-NUMBER: 20010001310
PGPUB-FILING-TYPE: new-utility
DOCUMENT-IDENTIFIER: US 20010001310 A1

TITLE: Bispecific antibodies for retargeting anticancer cytotoxic lymphocytes

PUBLICATION-DATE: May 17, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Weiner, George J.	Iowa City	IA	US	
Rokhlin, Oska W.	Coralville	IA	US	
Cohen, Michael B.	Iowa City	IA	US	

US-CL-CURRENT: 530/388.85; 435/326

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

3. Document ID: US 6300478 B1

L9: Entry 3 of 16 File: USPT Oct 9, 2001

US-PAT-NO: 6300478
DOCUMENT-IDENTIFIER: US 6300478 B1

TITLE: Antibodies to natural killer stimulatory factor

DATE-ISSUED: October 9, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Trinchieri; Giorgio	Wynnewood	PA		
Perussia; Bice	Philadelphia	PA		
Clark; Steven C.	Winchester	MA		
Wong; Gordon G.	Jamaica Plain	MA		
Hewick; Rodney	Lexington	MA		
Kobayashi; Michiko	Brookline	MA		

US-CL-CURRENT: 530/387.9; 530/387.1, 530/388.15, 530/388.24, 530/389.1, 530/389.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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4. Document ID: US 6207805 B1

L9: Entry 4 of 16 File: USPT Mar 27, 2001

US-PAT-NO: 6207805
DOCUMENT-IDENTIFIER: US 6207805 B1

TITLE: Prostate cell surface antigen-specific antibodies

DATE-ISSUED: March 27, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Weiner; George J.	Iowa City	IA		
Rokhlin; Oskar W.	Coralville	IA		
Cohen; Michael B.	Iowa City	IA		

US-CL-CURRENT: 530/388.85; 435/188, 435/326, 530/387.3, 530/388.1, 530/391.7

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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5. Document ID: US 6146837 A

L9: Entry 5 of 16 File: USPT Nov 14, 2000

US-PAT-NO: 6146837
DOCUMENT-IDENTIFIER: US 6146837 A

TITLE: Cyanidin compositions and therapeutic and diagnostic uses therefor

DATE-ISSUED: November 14, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
van de Winkel; Jan G. J.	Odijk			NLX

US-CL-CURRENT: 435/7.1; 530/370, 530/387.1, 530/388.22, 530/388.7, 530/388.9, 548/427, 548/455

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc
Image

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6. Document ID: US 5811523 A

L9: Entry 6 of 16 File: USPT Sep 22, 1998

US-PAT-NO: 5811523
DOCUMENT-IDENTIFIER: US 5811523 A

TITLE: Antibodies to natural killer stimulatory factor

DATE-ISSUED: September 22, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Trinchieri; Giorgio	Wynnewood	PA	19104	
Perussia; Bice	Philadelphia	PA	19146	
Clark; Steven C.	Winchester	MA	01890	
Wong; Gordon G.	Jamaica Plain	MA	02130	
Hewick; Rodney	Lexington	MA	02173	
Kobayashi; Michiko	Brookline	MA	02146	
Wolf; Stanley F.	Arlington	MA	02174	

US-CL-CURRENT: 530/387.9; 530/351, 530/387.1, 530/388.15, 530/388.24, 530/389.1, 530/389.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc
Image

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7. Document ID: US 5648467 A

L9: Entry 7 of 16 File: USPT Jul 15, 1997

US-PAT-NO: 5648467
DOCUMENT-IDENTIFIER: US 5648467 A

TITLE: Natural killer cell stimulatory factor

DATE-ISSUED: July 15, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Trinchieri; Giorgio	Wynnewood	PA		
Perussia; Bice	Philadelphia	PA		
Clark; Steven C.	Winchester	MA		
Wong; Gordon G.	Jamaica Plain	MA		
Hewick; Rodney	Lexington	MA		
Kobayashi; Michiko	Brookline	MA		
Wolf; Stanley F.	Arlington	MA		

US-CL-CURRENT: 530/351; 424/85.2, 435/69.52, 435/803, 530/416, 530/417

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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8. Document ID: US 5648072 A

L9: Entry 8 of 16 File: USPT Jul 15, 1997

US-PAT-NO: 5648072
DOCUMENT-IDENTIFIER: US 5648072 A

TITLE: Methods of inducing gamma interferon and stimulating blood cell populations using natural killer stimulatory factor

DATE-ISSUED: July 15, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Trinchieri; Giorgio	Wynnewood	PA		
Perussia; Bice	Philadelphia	PA		
Clark; Steven C.	Winchester	MA		
Kobayashi; Michiko	Brookline	MA		
Wong; Gordon G.	Jamaica Plain	MA		
Hewick; Rodney	Lexington	MA		
Wolf; Stanley F.	Arlington	MA		

US-CL-CURRENT: 424/85.2; 424/144.1, 424/198.1, 424/85.1, 424/85.5, 435/69.52, 514/12, 530/350, 530/351, 530/387.1, 530/388.22, 530/389.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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9. Document ID: US 5569454 A

L9: Entry 9 of 16 File: USPT Oct 29, 1996

US-PAT-NO: 5569454
DOCUMENT-IDENTIFIER: US 5569454 A

TITLE: Methods of treating infection using natural killer stimulatory factor

DATE-ISSUED: October 29, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Trinchieri; Giorgio	Wynnewood	PA		
Perussia; Bice	Philadelphia	PA		
Clark; Steven C.	Winchester	MA		
Wong; Gordon G.	Jamaica Plain	MA		
Hewick; Rodney	Lexington	MA		
Kobayashi; Michiko	Brookline	MA		
Wolf; Stanley F.	Arlington	MA		

US-CL-CURRENT: 424/85.2; 514/12, 514/2, 514/8, 514/885, 530/351

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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10. Document ID: US 5457038 A

L9: Entry 10 of 16 File: USPT Oct 10, 1995

US-PAT-NO: 5457038
DOCUMENT-IDENTIFIER: US 5457038 A

TITLE: Natural killer stimulatory factor

DATE-ISSUED: October 10, 1995

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Trinchieri; Giorgio	Wynnewood	PA		
Perussia; Bice	Philadelphia	PA		
Kobayashi; Michiko	Brookline	MA		
Clark; Steven C.	Winchester	MA		
Wong; Gordon G.	Jamaica Plain	MA		
Hewick; Rodney	Lexington	MA		

US-CL-CURRENT: 435/69.52; 435/235.1, 435/252.3, 435/252.33, 435/254.2, 435/320.1, 435/365.1, 435/69.1, 530/350, 536/23.5

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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Generate Collection | Print

Terms	Documents
L8 near antibod$4	16

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Search Results - Record(s) 11 through 16 of 16 returned.

11. Document ID: EP 739904 A1

L9: Entry 11 of 16 File: EPAB Oct 30, 1996

PUB-NO: EP000739904A1
DOCUMENT-IDENTIFIER: EP 739904 A1
TITLE: Bispecific reagents for aids therapy

PUBN-DATE: October 30, 1996

INVENTOR-INFORMATION:

NAME	COUNTRY
FANGER, MICHAEL W	US
GUYRE, PAUL M	US
DINCES, NATHAN B	US

INT-CL (IPC): C07 K 16/46; C07 K 16/28; C07 K 16/10; C12 N 5/00; A61 K 39/395; A61 K 35/12
EUR-CL (EPC): A61K047/48

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

12. Document ID: WO 9105871 A1

L9: Entry 12 of 16 File: EPAB May 2, 1991

PUB-NO: WO009105871A1
DOCUMENT-IDENTIFIER: WO 9105871 A1
TITLE: BISPECIFIC HETEROANTIBODIES WITH DUAL EFFECTOR FUNCTIONS

PUBN-DATE: May 2, 1991

INVENTOR-INFORMATION:

NAME	COUNTRY
FANGER, MICHAEL W	US
GUYRE, PAUL M	US
BALL, EDWARD D	US

US-CL-CURRENT: 435/FOR.101
INT-CL (IPC): A61K 35/14; C12N 5/08; C12P 21/08
EUR-CL (EPC): A61K035/14; C07K016/46

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

13. Document ID: WO 9100360 A1

L9: Entry 13 of 16 File: EPAB Jan 10, 1991

PUB-NO: WO009100360A1
DOCUMENT-IDENTIFIER: WO 9100360 A1
TITLE: BISPECIFIC REAGENTS FOR AIDS THERAPY

PUBN-DATE: January 10, 1991

INVENTOR-INFORMATION:

NAME	COUNTRY
FANGER, MICHAEL W	US
GUYRE, PAUL M	US
DINCES, NATHAN B	US

US-CL-CURRENT: 530/388.75
INT-CL (IPC): A61K 39/395; C12N 5/00; C12P 21/00
EUR-CL (EPC): A61K047/48; C07K014/16, C07K016/10 , C07K016/28 , C07K014/705 , C07K016/46

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

14. Document ID: WO 200202801 A1

L9: Entry 14 of 16 File: DWPI Jan 10, 2002

DERWENT-ACC-NO: 2002-154755
DERWENT-WEEK: 200220
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TITLE: Assaying function of Fc fragment in antibody, particularly in determining antibody-dependent cell-mediated cytotoxicity of antibody drugs with anti-cancer and antiviral action, e.g. in quality control

INVENTOR: SUGO, I

PRIORITY-DATA: 2000JP-0202622 (July 4, 2000)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 200202801 A1	January 10, 2002	J	022	C12Q001/02

INT-CL (IPC): A61 K 39/395; C07 K 16/00; C12 Q 1/02; G01 N 33/563

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Clip Img | Image

15. Document ID: DE 19905012 A1, EP 1025855 A1

L9: Entry 15 of 16 File: DWPI Aug 10, 2000

DERWENT-ACC-NO: 2000-492297
DERWENT-WEEK: 200045
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TITLE: Composition comprising two antibodies, useful for immunotherapy of autoimmune disease, one directed against T-cell receptor, the other against Fc gamma receptor

INVENTOR: KUMMER, U

PRIORITY-DATA: 1999DE-1005012 (February 8, 1999)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
DE 19905012 A1	August 10, 2000		000	A61K039/395
EP 1025855 A1	August 9, 2000	G	010	A61K039/395

INT-CL (IPC): A61 K 39/395; A61 P 37/06

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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16. Document ID: US 2001055592 A1, DE 19723690 A1, WO 9929731 A1, EP 951481 A1, US 2001009898 A1, JP 2001511821 W

L9: Entry 16 of 16 File: DWPI Dec 27, 2001

DERWENT-ACC-NO: 1998-194737
DERWENT-WEEK: 200206

TITLE: Use of Fc-gamma receptor antibodies - for treating amyotrophic lateral sclerosis

INVENTOR: SCHUBERT, W M; SCHUBERT, W

PRIORITY-DATA: 1996DE-1022491 (June 5, 1996), 1997WO-DE02883 (December 10, 1997), 1997EP-0951843 (December 10, 1997), 2001US-0801414 (March 8, 2001), 1999JP-0529595 (December 10, 1997), 2001US-0802305 (March 8, 2001)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 2001055592 A1	December 27, 2001		000	A61K039/395
DE 19723690 A1	March 26, 1998		005	A61K039/395
WO 9929731 A1	June 17, 1999	G	000	C07K016/28
EP 951481 A1	October 27, 1999	G	000	C07K016/28
US 2001009898 A1	July 26, 2001		000	A61K039/395
JP 2001511821 W	August 14, 2001		012	A61K038/00

INT-CL (IPC): A61 K 31/7088; A61 K 38/00; A61 K 39/00; A61 K 39/395; A61 K 48/00; A61 P 37/02; A61 P 43/00; C07 K 14/705 ; C07 K 16/28

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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L8 near antibod$4	16

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 NEWS  3  Jan 25  Searching with the P indicator for Preparations
 NEWS  4  Jan 29  FSTA has been reloaded and moves to weekly updates
 NEWS  5  Feb 01  DKILIT now produced by FIZ Karlsruhe and has a new update
                  frequency
 NEWS  6  Feb 19  Access via Tymnet and SprintNet Eliminated Effective 3/31/02
 NEWS  7  Mar 08  Gene Names now available in BIOSIS
 NEWS  8  Mar 22  TOXLIT no longer available
 NEWS  9  Mar 22  TRCTHERMO no longer available
 NEWS 10  Mar 28  US Provisional Priorities searched with P in CA/CAplus
                  and USPATFULL
 NEWS 11  Mar 28  LIPINSKI/CALC added for property searching in REGISTRY
 NEWS 12  Apr 02  PAPERCHEM no longer available on STN.  Use PAPERCHEM2 instead.

 NEWS EXPRESS  February 1 CURRENT WINDOWS VERSION IS V6.0d,
               CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
               AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
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 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
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                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

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                                                       ENTRY    SESSION
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                  frequency
 NEWS  6  Feb 19  Access via Tymnet and SprintNet Eliminated Effective 3/31/02
 NEWS  7  Mar 08  Gene Names now available in BIOSIS
 NEWS  8  Mar 22  TOXLIT no longer available
 NEWS  9  Mar 22  TRCTHERMO no longer available
 NEWS 10  Mar 28  US Provisional Priorities searched with P in CA/CAplus
                  and USPATFULL
 NEWS 11  Mar 28  LIPINSKI/CALC added for property searching in REGISTRY
 NEWS 12  Apr 02  PAPERCHEM no longer available on STN.  Use PAPERCHEM2 instead.
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              CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
              AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
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FULL ESTIMATED COST                                    0.21        0.21

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=> s fcgammaR1
L1            7 FCGAMMAR1

=> s fc (1N) gamma (1N) R1
L2           65 FC (1N) GAMMA (1N) R1

=> s fc (1N) gamma (1N) RI
L3         1957 FC (1N) GAMMA (1N) RI

=> s cd64
L4          982 CD64

=> s l1 and l2 and l3 and l4
L5            0 L1 AND L2 AND L3 AND L4

=> s l1 or l2 or l3 or l4
L6         2547 L1 OR L2 OR L3 OR L4

=> s l6 (P) antibod?
L7         1130 L6 (P) ANTIBOD?

=> s l7 (P) administ?
L8           54 L7 (P) ADMINIST?

=> dup rem l8
PROCESSING COMPLETED FOR L8
L9            26 DUP REM L8 (28 DUPLICATES REMOVED)

=> dis l9 1-26 ibib abs

L9   ANSWER 1 OF 26     MEDLINE                              DUPLICATE 1
ACCESSION NUMBER:    2001463302     MEDLINE
DOCUMENT NUMBER:     21384768    PubMed ID: 11493456
TITLE:               Therapeutic efficacy of intravenous immunoglobulin
                     preparations depends on the immunoglobulin G dimers:
                     studies in experimental immune thrombocytopenia.
AUTHOR:              Teeling J L; Jansen-Hendriks T; Kuijpers T W; de Haas M;
                     van de Winkel J G; Hack C E; Bleeker W K
CORPORATE SOURCE:    Central Laboratory of the Netherlands Red Cross Blood
                     Transfusion Service, Academical Medical Center, University
                     of Amsterdam, The Netherlands.
SOURCE:              BLOOD, (2001 Aug 15) 98 (4) 1095-9.
                     Journal code: A8G; 7603509. ISSN: 0006-4971.
PUB. COUNTRY:        United States
                     Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH:         200109
ENTRY DATE:          Entered STN: 20010820
                     Last Updated on STN: 20010924
                     Entered Medline: 20010920

AB   The clinical benefit of intravenous immunoglobulin (IVIG) preparations in
     the treatment of immune thrombocytopenic purpura (ITP) is supposed to be
     mediated by blockade of Fc gamma receptor--bearing phagocytes. In 2
     experimental models for ITP, it is shown that the therapeutic efficacy of
     IVIG preparations is related to the IgG dimer content present in these
     preparations. A rat monoclonal antibody (mAb; MWReg30) directed
     to the murine platelet-specific integrin alpha(IIb)beta(3) (gpIIb/IIIa)
     was administered intraperitoneally either as bolus injection or
     continuous infusion. With bolus injection, the circulating platelet count
     dropped to almost zero within 3 hours. Pretreatment with cobra venom
     factor did not affect platelet depletion, whereas pretreatment with
     anti-Fc gamma RII/III mAb 2.4G2 or IVIG greatly reduced platelet
     clearance. With continuous infusion, platelet numbers reached a steady
     state after 4 days, at approximately 25% of control. This reduction in
     platelets was, however, not observed in mice deficient for the FcR
     gamma-chain, lacking Fc gamma RI, Fc
     gamma RIII, and Fc gamma RIII(-/-) mice. Infusion of a single dose
     of IVIG with a high IgG dimer content on the 4th day--ie, mimicking
     therapeutic administration--resulted in a platelet increase for
     several days. IVIG predominantly consisting of monomeric IgG had no effect
     on platelet numbers. In conclusion, continuous infusion of MWReg30 induces
     thrombocytopenia in mice by enhancing Fc gamma receptor--mediated
```

clearance of platelets. In this model, it is shown that IgG dimers present in IVIG preparations are responsible for the increase in platelet counts. (Blood. 2001;98:1095-1099)

L9 ANSWER 2 OF 26 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2
ACCESSION NUMBER: 2001:826584 CAPLUS
TITLE: IgG2a-mediated enhancement of antibody responses is dependent on FcR.gamma.+ bone marrow-derived cells
AUTHOR(S): De Stahl, T. Diaz; Heyman, B.
CORPORATE SOURCE: Department of Genetics and Pathology, Uppsala University, Uppsala, Swed.
SOURCE: Scand. J. Immunol. (2001), 54(5), 495-500
CODEN: SJIMAX; ISSN: 0300-9475
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Antibodies** (Ab) **administered** in complex with antigens (Ag) have the capacity to regulate the out-coming specific immune response. Primary immunization with complexes of bovine serum albumin-2,4,6-trinitrophenyl (BSA-TNP) and Ig (Ig)G2a anti-TNP induced a significant enhancement of IgG1 and IgG2a BSA-specific Ab response compared to immunization with the Ag alone. Enhancement was absent in nude mice, demonstrating the requirement of T cells for this regulation. Secondary immunization with BSA alone in mice previously primed with BSA-TNP/IgG2a led to a dramatic increase of Ab prodn., showing that immune complexes are efficient inducers of immunol. memory. IgG-mediated enhancement of Ab responses has previously been shown to be impaired in mice lacking **Fc.gamma.RI**, **Fc.gamma.**RIII and Fc.epsilon.RI owing to gene targeting of the common FcR.gamma. subunit (FcR.gamma.-/-). Here we show that enhancement after immunization with BSA-TNP/IgG2a complexes is restored in irradiated FcR.gamma.-/- recipients transferred with wild-type (FcR.gamma.+/+) bone marrow (BM) cells. In contrast, no enhancement is seen in FcR.gamma.+/+ irradiated animals reconstituted with FcR.gamma.-/- BM cells. We conclude that IgG2a-mediated enhancement of Ab responses is dependent on the presence of **Fc.gamma.RI** and/or Fc.gamma.RIII on BM-derived cells and that the presence of these receptors on the radioresistant follicular dendritic cell is not essential.
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 26 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 3
ACCESSION NUMBER: 2001:311246 CAPLUS
DOCUMENT NUMBER: 135:356512
TITLE: IgE-mediated suppression of primary antibody responses in vivo
AUTHOR(S): Karlsson, M. C. I.; Diaz De Stahl, T.; Heyman, B.
CORPORATE SOURCE: Department of Genetics and Pathology, Rudbeck Laboratory, Uppsala University, Uppsala, SE-751 85, Swed.
SOURCE: Scandinavian Journal of Immunology (2001), 53(4), 381-385
CODEN: SJIMAX; ISSN: 0300-9475
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The ability of IgG to feedback suppress **antibody** (Ab) responses is a well known property clin. used to prevent hemolytic disease of newborns. The authors recently found that IgG was able to suppress the primary Ab response to sheep red blood cells (SRBC) in mice lacking the known Fc-receptors for IgG. In addn., IgE and F(ab')2 fragments of IgG were able to suppress the response to SRBC in wild-type mice. These results suggested that the IgG-mediated suppression can take place independently of the IgG (Fc) portion and that masking of the epitopes is an important mechanism. In the present report the authors investigated whether the suppression caused by IgE is Fc-dependent. Monoclonal IgE anti-2,4,6-trinitrophenyl (TNP), **administered** with TNP-coupled SRBC (SRBC-TNP), can induce an efficient suppression in mice lacking **Fc.gamma.RI** + RIII + Fc.epsilon.RI (owing to the lack of the common .gamma. chain, FcR.gamma.), Fc.gamma.RIIB or Fc.epsilon.RII (CD23). Because the known IgE-binding receptors are Fc.epsilon.**RI**, CD23, **Fc.gamma.**RIIB and Fc.gamma.RIII, the results suggest that also the IgE-mediated suppression can take place independently of the Fc-receptors. A slightly less efficient suppression in CD23-deficient animals, suggests a minor involvement of this receptor.
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 26 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 4
ACCESSION NUMBER: 2001:715454 CAPLUS
DOCUMENT NUMBER: 136:19011
TITLE: Subcutaneous administration of interleukin-2 triggers Fc.gamma. receptor I expression on human peripheral blood neutrophils in solid and hematologic malignancies
AUTHOR(S): Sconocchia, Giuseppe; Cococcetta, Nella Y.; Campagnano, Laura; Amadori, Sergio; Iorio, Beniamino; Boffo, Vittorio; Ferdinandi, Vincenzo; Del Principe, Ilaria; Adorno, Domenico; Casciani, Carlo U.
CORPORATE SOURCE: Institute of Tissue Typing and Dialysis, Consiglio Nazionale delle Ricerche, University "Tor Vergata", Rome, Italy
SOURCE: Journal of Immunotherapy (2001), 24(4), 374-383
CODEN: JOIMF8; ISSN: 1053-8550
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Freshly isolated human polymorphonuclear cells (PMNCs) constitutively express Fc.gamma. receptor (Fc.gamma.R) II and Fc.gamma.RIII on the cell surface but not **Fc.gamma.RI**. Cytokines such as interferon-.gamma. (IFN.gamma.), granulocyte-macrophage colony-stimulating factor (CSF), and granulocyte-CSF trigger **Fc.gamma.RI** expression on (PMNCs). Because PMNCs express interleukin (IL)-2 receptor, we investigated whether IL-2 can induce **Fc.gamma.RI** expression on PMNCs isolated from IL-2-treated metastatic renal cell carcinoma (MRCC) and low-grade non-Hodgkin lymphoma (LGNHL) patients. Pretherapy flow cytometry anal. of Fc receptors on PMNCs did not show **Fc.gamma.RI** expression. Interestingly, 3 days after therapy, PMNCs displayed a detectable amt. of **Fc.gamma.RI** on the cell surface. Kinetic studies on the in vivo effects of IL-2 on MRCC patients showed that **Fc.gamma.RI** was transiently

expressed, starting within 3-6 days of therapy, remaining expressed for 10-15 days, and rapidly declining, whereas such expression remained stable for months in LGNHL patients. In contrast, Fc.gamma.RII was not affected. In addn., **Fc.gamma.RI**+ PMNCs coated in vitro with a bispecific **antibody** Fab anti-**Fc.gamma** .**RI** .times. anti-HER-2/neu formed intercellular conjugates with a human HER-2/neu-transfected 3T3 cell line (HER-2/neu-3T3). Interleukin-2 treatment increased the no. of Fc.gamma.RIII low eosinophils, leading to a change in Fc.gamma.RIII distribution among granulocyte cell subsets. In vitro IL-2 treatment of purified PMNCs failed to generate **Fc.gamma.RI** expression, suggesting that IL-2 indirectly causes **Fc.gamma**. **RI** expression. During the IL-2 **administration**, we did not observe significant changes in IFN.gamma. serum level. In conclusion, our observation may be used to potentiate the antitumor effects of IL-2 in novel immunotherapy regimens, perhaps by redirecting **Fc**. **gamma.RI**+ PMNCs against cancer cells by heteroconjugate **antibodies** and monitoring the biol. activity of s.c. IL-2 in cancer patients.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 26 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 5

ACCESSION NUMBER: 2001:129404 CAPLUS
DOCUMENT NUMBER: 134:324925
TITLE: Bispecific antibody-targeted phagocytosis of HER-2/neu expressing tumor cells by myeloid cells activated in vivo
AUTHOR(S): Wallace, P. K.; Kaufman, P. A.; Lewis, L. D.; Keler, T.; Givan, A. L.; Fisher, J. L.; Waugh, M. G.; Wahner, A. E.; Guyre, P. M.; Fanger, M. W.; Ernstoff, M. S.
CORPORATE SOURCE: Department of Microbiology, HB7556, Dartmouth Medical School and the Immunology Immunotherapy Program of the Norris Cotton Cancer Center, Lebanon, NH, 03756, USA
SOURCE: Journal of Immunological Methods (2001), 248(1-2), 167-182
CODEN: JIMMBG; ISSN: 0022-1759
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Studies from the authors' lab. and others have established that both mononuclear phagocytes and neutrophils mediate very efficient cytotoxicity when targeted through Fc receptors using a suitable monoclonal or bispecific **antibody** (BsAb). Crosslinking an Fc receptor for IgG (Fc.gamma.R) triggers multiple anti-tumor activities including superoxide generation, cytokine and enzyme release, phagocytosis and **antibody** -dependent cellular cytotoxicity (ADCC). In this report, using unfractionated leukocytes and two color flow cytometric anal., the authors describe the phagocytic capacity of peripheral blood polymorphonuclear cells (PMN) and monocytes isolated from patients enrolled in a phase I clin. trial of MDX-H210 given in combination with IFN.gamma.. MDX-H210 is a BsAb targeting the myeloid trigger mol. **Fc.gamma**. **RI** and the HER-2/neu proto-oncogene product overexpressed on a variety of adenocarcinomas. In this trial, cohorts of patients received escalating doses of MDX-H210 3 times per wk for 3 wk. Interferon-.gamma. (IFN.gamma.) was given 24 h prior to each BsAb infusion. Our results demonstrate that monocytes from these patients were inherently capable of phagocytosing the HER-2/neu pos. SK-BR-3 cell line and that addn. of MDX-H210 into the assay significantly enhanced the no. of targets phagocytosed. Two days after **administration** of an immunol. active dose of MDX-H210 (10 mg/m2), monocytes from these patients were able to phagocytose greater amts. of target cell material, indicating that these cells remained armed with functionally sufficient BsAb for at least 48 h. PMN from these patients very efficiently mediated phagocytosis through **Fc.gamma.RI** after being treated with IFN.gamma., but not before. The authors conclude that phagocytosis is not only an efficient mechanism of myeloid cell-mediated cytotoxicity, but may also be a mechanism by which antigens from phagocytosed cells can enter a professional antigen presenting cell for processing and presentation.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 26 MEDLINE DUPLICATE 6

ACCESSION NUMBER: 2001159755 MEDLINE
DOCUMENT NUMBER: 21126046 PubMed ID: 11223076
TITLE: Pharmacokinetic-pharmacodynamic relationships of the bispecific antibody MDX-H210 when administered in combination with interferon gamma: a multiple-dose phase-I study in patients with advanced cancer which overexpresses HER-2/neu.
AUTHOR: Lewis L D; Cole B F; Wallace P K; Fisher J L; Waugh M; Guyre P M; Fanger M W; Curnow R T; Kaufman P A; Ernstoff M S
CORPORATE SOURCE: Department of Medicine, Dartmouth Medical School and The Norris Cotton Cancer Center, Lebanon, NH 03756, USA.. lionel.d.lewis@dartmouth.edu
CONTRACT NUMBER: CA-23108 (NCI)
RO1 CA65963 (NCI)
SOURCE: JOURNAL OF IMMUNOLOGICAL METHODS, (2001 Feb 1) 248 (1-2) 149-65.
Journal code: IFE; 1305440. ISSN: 0022-1759.
PUB. COUNTRY: Netherlands
(CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 20010410
Last Updated on STN: 20010410
Entered Medline: 20010405

AB INTRODUCTION: MDX-H210 is a Fab'xFab' bispecific **antibody** (BsAb) constructed chemically by crosslinking Fab' mAb 520C9 (anti-HER-2/neu) and Fab' mAbH22 (anti-**CD64**). STUDY DESIGN AND OBJECTIVES: This was a dose escalation study of intravenous MDX-H210 (1-70 mg/m(2)), preceded 24 h beforehand by subcutaneous IFNgamma (50 microg/m(2) to up-regulate FcgammaRI) **administered** three times a week for 3 weeks. We investigated the pharmacokinetic-pharmacodynamic relationships between MDX-H210 C(max) and AUC and (i) MDX-H210 binding to peripheral blood monocytes and neutrophils, (ii) the peak plasma G-CSF, IL-6, IL-8 and TNFalpha concentrations, and (iii) the observed clinical toxicity. RESULTS: 23 patients (19F:4M; median age 51.5; range 25-72 y) with advanced HER-2/neu positive cancers (19 breast, three prostate and one

lung) were studied. Plasma MDX-H210 concentrations over time, circulating numbers of monocytes and neutrophils, percent saturation of monocyte and neutrophil FcgammaRI, and plasma concentrations over time of G-CSF, IL-6, IL-8 and TNFalpha were measured and clinical toxicity monitored. The E(max) pharmacodynamic model best fitted the relationship of MDX-H210 C(max) and the maximum percent saturation of both monocytes (E(max)=74.6; EC(50)=0.9 microg/ml) and neutrophils (E(max)=66.2; EC(50)=2.3 microg/ml) on the first day of treatment. On the last day of treatment, day 19, these parameters were E(max)=57.0% and EC(50)=0.46 microg/ml for monocytes and E(max)=61.9% and EC(50)=0.26 microg/ml for neutrophils. No positive relationship was defined between the log MDX-H210 C(max) and the log peak plasma IL-6, G-CSF, TNF or IL-8 concentrations on day 1. On day 19 these plasma cytokine concentrations were undetectable post MDX-H210 therapy. There was no consistent relationship between MDX-H210 C(max) and the observed clinical toxicities. CONCLUSIONS: These data suggest that MDX-H210 C(max) and AUC could be related by the E(max) model to maximum percent FcgammaRI saturation on circulating monocytes and neutrophils in the patients studied. After day 1, the post MDX-H210 therapy cytokine response attenuated over time, consistent with desensitization. We did not find a relationship between log MDX-H210 C(max) and peak plasma cytokine concentrations or clinical toxicities.

L9 ANSWER 7 OF 26 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 7
ACCESSION NUMBER: 2001:570793 CAPLUS
DOCUMENT NUMBER: 135:298857
TITLE: G-CSF: Mode of action and antiinfective activities
AUTHOR(S): Rouveix, B.; Giroud, J.-P.; Levacher, M.
CORPORATE SOURCE: Service de Pharmacologie Clinique, CNRS - URA 1534, Hopital Cochin, Paris, Fr.
SOURCE: Antibiotiques (2001), 3(2), 83-89
CODEN: ANTBFQ; ISSN: 1294-5501
PUBLISHER: Masson Editeur
DOCUMENT TYPE: Journal; General Review
LANGUAGE: French

AB A review, with 57 refs. Infectious diseases remain a major cause of morbidity and mortality. Alteration of natural mechanisms of defense against infection, emergence of antibiotic resistant bacteria and limited development of newer antiinfectives have led to the development of therapeutic adjuvants. Hematopoietic growth factors including granulocyte stimulating factor (G-CSF) have been used in prophylaxis and treatment of febrile episodes in neutropenic patients treated by anti-cancer chemotherapy. For >10 yr, hundreds thousands patients have been treated by G-CSF by a once daily s.c. injection, with an overall good tolerance, to reduce the duration of neutropenia and its assocd. complications. G-CSF stimulates neutrophils' prodn., and activates their anti-bacterial functions in vitro and in vivo. Prodn. of superoxide anions is facilitated, as well as migration, phagocytosis and **Antibody** Dependent Cytotoxicity (ADCC phenomenon). Bactericidal effect is increased against many organisms such as Gram pos. or Gram neg. bacteria and fungi. Expression and affinities of surface. Antigens are modulated (Fc.**gamma**.RIII, **Fc.gamma.RI**, L-selectin, CD11b/CD18,CD14, CD66b). In addn., neutrophils' survival is increased with delayed apoptosis. The overall effect suggests that natural organism defenses are stimulated by G-CSF. More recently, data from human neutrophils have clearly shown that G-CSF **administered** with antibiotics increased in vivo intracellular concns. of the antibiotic, acting concomitantly in a synergistic bactericidal effect. Such an antinfective potential effect of G-CSF has been evaluated in many animal models of peritonitis, pneumonia, endocarditis and septicemia. A global favorable effect has been reported regarding bactericidal effect of neutrophils and animal survival, although the limits of such effects refer to tech. restricted conditions. These results justify and encourage the use of G-CSF assocd. with antibiotics in the treatment of acute community acquired or hospital acquired non-neutropenic infections.

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 26 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:722927 CAPLUS
DOCUMENT NUMBER: 131:335816
TITLE: Reversal of proinflammatory response by ligating the macrophage Fc.gamma.RI receptor
INVENTOR(S): Mosser, David M.; Sutterwala, Fayyaz S.
PATENT ASSIGNEE(S): Temple University - of the Commonwealth System of Higher Education, USA
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9956777	A1	19991111	WO 1999-US9269	19990429
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9938710	A1	19991123	AU 1999-38710	19990429
EP 1082137	A1	20010314	EP 1999-921519	19990429
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1998-84385P P 19980506
WO 1999-US9269 W 19990429

AB Ligation of the Fc.gamma. receptor type I (**Fc.gamma.RI**) on IL-10-producing cells leads to a selective upregulation of IL-10 prodn., which in turn induces a marked suppression of IL-12 biosynthesis by IL-12-producing cells, particularly macrophages. The ligation of the **Fc.gamma.RI** receptor thus down-modulates IL-12 prodn. via a mechanism that is dependent on macrophage-derived IL-10. Agents for ligating **Fc.gamma.RI** comprise, for example, multivalent **antibodies** which bind the **Fc.gamma.RI** receptor, immune complexes comprising **antibodies** which contain the Fc region of IgG, and IgG multimers, preferably IgG dimers and trimers. The ligating agent may be **administered** to therapeutically inhibit proinflammatory immune responses. In particular, the ligating agent may

be **administered** to treat or prevent endotoxic shock assocd. with bacterial endotoxemia, and to treating autoimmune disorders.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 26 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 8
ACCESSION NUMBER: 1999:180945 CAPLUS
DOCUMENT NUMBER: 130:336683
TITLE: Efficient IgG-mediated suppression of primary antibody responses in Fc.gamma. receptor-deficient mice
AUTHOR(S): Karlsson, Mikael C. I.; Wernersson, Sara; De Stahl, Teresita Diaz; Gustavsson, Susanne; Heyman, Birgitta
CORPORATE SOURCE: Department of Genetics and Pathology, Unit of Pathology, Uppsala University, Uppsala, S-751 85, Swed.
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1999), 96(5), 2244-2249
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB IgG **antibodies** can suppress >99% of the **antibody** response against the antigen to which they bind. This is used clin. to prevent rhesus-neg. (Rh-) women from becoming immunized against Rh+ erythrocytes from their fetuses. The suppressive mechanism is poorly understood, but it has been proposed that IgG/erythrocyte complexes bind to the inhibitory Fc receptor for IgG (Fc.gamma.RIIB) on the B cell surface, thereby triggering neg. signals that turn off the B cell. The authors show that IgG induces the same degree of suppression of the response to sheep erythrocytes in animals lacking the known IgG-binding receptors Fc.**gamma**.RIIB, **Fc.gamma.RI** + III, **Fc.gamma.RI** + IIB + III, and FcRn (the neonatal Fc receptor) as in wild-type animals. Reinvestigation of the ability of F(ab')2 fragments to suppress **antibody** responses demonstrated that they were nearly as efficient as intact IgG. In addn., monoclonal IgE also was shown to be suppressive. Thus, IgG inhibits **antibody** responses via Fc-independent mechanisms, most likely by masking of antigenic epitopes, thereby preventing B cells from binding and responding to antigen. In agreement with this, the authors show that T cell priming is not abolished by passively **administered** IgG. The results have implications for the understanding of in vivo regulation of **antibody** responses and Rh prophylaxis.
REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 10 OF 26 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 1999332518 MEDLINE
DOCUMENT NUMBER: 99332518 PubMed ID: 10404439
TITLE: A pilot trial of GM-CSF and MDX-H210 in patients with erbB-2-positive advanced malignancies.
AUTHOR: Posey J A; Raspet R; Verma U; Deo Y M; Keller T; Marshall J L; Hodgson J; Mazumder A; Hawkins M J
CORPORATE SOURCE: Department of Medicine, Lombardi Cancer Center, Georgetown University Medical Center, Washington, D.C., USA.
SOURCE: JOURNAL OF IMMUNOTHERAPY, (1999 Jul) 22 (4) 371-9.
Journal code: CUQ; 9706083.
PUB. COUNTRY: United States
(CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199909
ENTRY DATE: Entered STN: 19991012
Last Updated on STN: 20000303
Entered Medline: 19990928
AB MDX-H210 is a chemically, cross-linked, half-humanized bispecific **antibody** composed of F(ab') fragment from monoclonal **antibody** (mAb) H22 that binds to the high-affinity receptor **Fc gamma RI** and F(ab') of mAb 520C9 that recognizes the erbB-2 (HER2/neu) oncoprotein. In a previous trial, the murine bispecific, MDX-210 at a dose of 7 mg/m2, was well tolerated and activated monocytes and macrophages in vivo in doses as low as 0.35 mg/m2. In our multidose trial, granulocyte-macrophage colony-stimulating factor, which increases and activates potential effector cells, was given on days 1-4 at 250 micrograms/m2 s.c. and MDX-H210 was given on day 4 weekly for 4 consecutive weeks. Thirteen patients were treated at dose levels of 1, 3.5, 7, 10, 15, and 20 mg/m2 without dose-limiting toxicity. Fever, chills, and rigors occurred during and up to 2 h postinfusion and correlated with the time to peak levels of tumor necrosis factor-alpha (median 88.2 pg/ml; range 15.6-887 pg/ml) and interleukin-6 (median 371 pg/ml; range 175-2,149 pg/ml). By the fourth consecutive week of treatment the side effects and cytokine levels decreased significantly. Human antibispecific **antibody** (HABA) levels were increased by 200- to 500-fold above pretreatment levels in 5 of 11 evaluable patients after 3 weeks of treatment. The monocyte and granulocyte population increased on days 4 and 11 (median 44%; range 18-68% and 42%; 19-71%), respectively, for monocytes and (60%; 43-75% and 74%; 54-82%) on days 4 and 11 for granulocytes. There was a significant decrease in the monocyte populations immediately after MDX-H210 **administration** (median decrease 73%; range 42-94%) and (52%; 12-72%) on days 4 and 11, respectively. Ten patients completed 4 weeks of treatment. One patient had a 48% reduction in an index lesions and six patients had stable disease at the time of evaluation. Three patients progressed before the fourth week. The therapy was generally well tolerated with toxicity, primarily, limited to the days of treatment.

L9 ANSWER 11 OF 26 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 2000065744 MEDLINE
DOCUMENT NUMBER: 20065744 PubMed ID: 10598685
TITLE: Specific targeting immunotherapy of cancer with bispecific antibodies.
AUTHOR: Kudo T; Suzuki M; Katayose Y; Shinoda M; Sakurai N; Kodama H; Ichiyama M; Takemura S; Yoshida H; Saeki H; Saijyo S; Takahashi J; Tominaga T; Matsuno S
CORPORATE SOURCE: Cell Resource Center for Biomedical Research, Institute of Development, Aging and Cancer, Tohoku University, Sendai, Japan.. j23700@gen.cc.tohoku.ac.jp
SOURCE: TOHOKU JOURNAL OF EXPERIMENTAL MEDICINE, (1999 Aug) 188 (4) 275-88. Ref: 27
Journal code: VTF; 0417355. ISSN: 0040-8727.
PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000124
Last Updated on STN: 20000124
Entered Medline: 20000112

AB In order to enhance cell mediated cytotoxicity, bispecific **antibodies** (BsAbs), molecules combining two or more **antibodies** with different antigenic specificities, have been developed as new agents for immunotherapy. Our recent studies revealed that simultaneous **administration** of two kinds of BsAbs (anti-tumor x anti-CD3 plus anti-tumor x anti-CD28) together with lymphokine activated killer cells with a T cell phenotype (T-LAK cells) inhibited growth of human xenotransplanted tumors in severe combined immunodeficient (SCID) mice, while single BsAb was without effect. Three kinds of BsAbs (anti-tumor x anti-CD3, anti-tumor x anti-CD28, anti-tumor x anti-CD2) showed the highest cytotoxicity against tumor cells when given simultaneously with T-LAK cells or peripheral blood mononuclear cells in vitro and in vivo. BsAbs can be preserved for immediate application, while cytotoxic T lymphocytes (CTLs) must be made-to-order, and are time-consuming to prepare. Tumor associated antigens, such as MAGE antigens, SART antigens, MUC1 antigen, c-erbB 2 antigen or cancer/testis antigens can be served to target antigens for BsAb production. By conjugation with **antibodies** to effector cells (anti-CD3, anti-CD28, anti-CD16, anti-**CD64**, anti-CD89 or anti-CD2), many kinds of BsAbs can be produced to cover most types of cancers from different organs. Therefore this strategy might be ubiquitously applicable to most malignancies.

L9 ANSWER 12 OF 26 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:122641 CAPLUS
DOCUMENT NUMBER: 130:152290
TITLE: In vivo administration of granulocyte colony-stimulating factor increases the surface expression of sialyl-Lewisx on neutrophils in healthy volunteers
AUTHOR(S): Ohsaka Akimichi; Saionji, Katsu
CORPORATE SOURCE: Dep. Internal Medine, Div. Hematology, Hitachi General Hospital, Hitachi, 317, Japan
SOURCE: Acta Haematol. (1999), Volume Date 1998, 100(4), 187-190
CODEN: ACHAAH; ISSN: 0001-5792
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors examd. the in vivo effect of granulocyte colony-stimulating factor (G-CSF) on the surface expression of putative counterligands for endothelial selectins on neutrophils in healthy. G-CSF (50 .mu.g/m2/day) was **administered** s.c. to healthy for 4 days. The expression of surface antigens on neutrophils was detd. by flow cytometry and monoclonal **antibodies**. G-CSF **administration** increased the no. of leukocytes, mainly of neutrophils, which was assocd. with an increase in the expression of the high-affinity Fc receptor for IgG (FcRI, **CD64**) and CD14 G-CSF **administration** increased the no. of leukocytes, mainly of neutrophils, which was assocd. with an increase in the expression of the high-affinity Fc receptor for IgG (FcRI, **CD64**) and CD14 on neutrophils. G-CSF **administration** decreased the surface expression of L-selectin on neutrophils, whereas it increased the expression of sialyl-Lewisx but not Lewisx on neutrophils. These findings suggest that G-CSF participates in the neutrophil-endothelial cell interactions in viva by modulating the expression of adhesion mols. and ligands for endothelial selectins on neutrophils.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 13 OF 26 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 11
ACCESSION NUMBER: 1999:107240 CAPLUS
DOCUMENT NUMBER: 130:138268
TITLE: Cellular requirements for the monoclonal antibody-mediated eradication of an established solid tumor
AUTHOR(S): Dyall, Ruben; Vasovic, Ljiljana V.; Clynes, Raphael A.; Nikolic-Zugic, Janko
CORPORATE SOURCE: Laboratory T Cell Development, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA
SOURCE: Eur. J. Immunol. (1999), 29(1), 30-37
CODEN: EJIMAF; ISSN: 0014-2980
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Following s.c. implantation, the murine lymphoma E.G7 [a variant of EL-4, transfected with the chicken ovalbumin (OVA) gene] up-regulates the CD4 mol. The authors previously showed that the **administration** of an anti-CD4 monoclonal **antibody** (mAb) to EG.7-bearing mice leads to a rapid and complete regression of large established tumors. This tumor regression was shown to require both CD8+ cells and functional Fc.gamma. receptors (Fc.gamma.R), as it failed to occur in mice depleted of CD8 cells, or mice genetically deficient in **Fc.gamma** .**RI**/III (.gamma.-/- mice). Using adoptive transfer, the authors now show that the Fc.gamma.R+ cells required for this regression are the CD11b+ (phagocytic) cells. Expts. using peptide tolerization demonstrated that the crit. CD8 CTL population in this model is tumor specific. Anal. of tumors at various stages of regression revealed a massive CD11b+ Fc.gamma.R+ and a marginal CD8 infiltration. In the presence of the CTL determinant OVA-8 on tumor cells and of the antitumor mAb, this CD8 infiltration became remarkable, and correlated with tumor regression. These results identify the specific cellular effectors essential for the mAb-mediated tumor regression, and suggest that Fc.gamma.R-activated macrophages induced an expansion of tumor-eliminating CTL.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 14 OF 26 MEDLINE DUPLICATE 12
ACCESSION NUMBER: 1999249563 MEDLINE
DOCUMENT NUMBER: 99249563 PubMed ID: 10235484
TITLE: A phase I study of a HER2/neu bispecific antibody with granulocyte-colony-stimulating factor in patients with metastatic breast cancer that overexpresses HER2/neu.
AUTHOR: Pullarkat V; Deo Y; Link J; Spears L; Marty V; Curnow R; Groshen S; Gee C; Weber J S
CORPORATE SOURCE: USC/Norris Comprehensive Cancer Center, Los Angeles, CA

90049, USA.
SOURCE: CANCER IMMUNOLOGY, IMMUNOTHERAPY, (1999 Apr) 48 (1) 9-21.
Journal code: CN3; 8605732. ISSN: 0340-7004.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
(CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990614
Last Updated on STN: 20000303
Entered Medline: 19990601

AB A phase I study of escalating doses of humanized bispecific **antibody** (bsAb) MDX-H210 with granulocyte-colony-stimulating factor (G-CSF) was conducted in patients with metastatic breast cancer that overexpressed HER2/neu. The main objectives of the study were to define the maximal tolerated dose (MTD) of MDX-H210 when combined with G-CSF, to measure the pharmacokinetics of MDX-H210 when **administered** with G-CSF, and to determine the toxicity, biological effects and possible therapeutic effect of MDX-H210 with G-CSF. MDX-H210 is a F(ab)' x F(ab)' humanized bispecific murine **antibody** that binds to both HER2/neu and the **FcgammaRI** receptor (**CD64**), and was **administered** intravenously weekly for three doses followed by a 2-week break and then three more weekly doses. A total of 23 patients were treated, and doses were escalated from 1 mg/m2 to 40 mg/m2 with no MTD reached. The toxicity of the bsAb + G-CSF combination was modest, with no dose-limiting toxicity noted: 19 patients had fevers, 7 patients had diarrhea, and 3 patients had allergic reactions that did not limit therapy. The beta-elimination half-life varied from 4 h to 8 h at doses up to 20 mg/m2. Significant release of cytokines interleukin-6, G-CSF, and tumor necrosis factor alpha was observed after **administration** of bsAb. Circulating monocytes disappeared within 1 h of bsAb infusion, which correlated with binding of bsAb, noted by flow-cytometric analysis. Significant levels of human anti-(bispecific **antibody**) were measured in the plasma of most patients by the third infusion. No objective clinical responses were seen in this group of heavily pre-treated patients.

L9 ANSWER 15 OF 26 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 13
ACCESSION NUMBER: 1998:114986 CAPLUS
DOCUMENT NUMBER: 128:216267
TITLE: Antibody-mediated modulation of Cryptococcus neoformans infection is dependent on distinct Fc receptor functions and IgG subclasses
AUTHOR(S): Yuan, Ruirong; Clynes, Raphael; Oh, Jin; Ravetch, Jeffrey V.; Scharff, Matthew D.
CORPORATE SOURCE: Department of Cell Biology of the Albert Einstein College of Medicine, Bronx, NY, 10461, USA
SOURCE: J. Exp. Med. (1998), 187(4), 641-648
CODEN: JEMEAV; ISSN: 0022-1007
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Coupling of an **antibody** response to effector cells through the Fc region of **antibodies** is a fundamental objective of effective vaccination. We have explored the role of the Fc receptor system in a murine model of Cryptococcus neoformans protection by infecting mice deleted for the common .gamma. chain of FcRs. Passive **administration** of an IgG1 mAb protects FcR.gamma.+/- mice infected with C. neoformans, but fails to protect FcR.gamma.-/- mice, indicating that the .gamma. chain acting through **Fc.gamma**. **RI** and/or III is essential for IgG1-mediated protection. In contrast, passive **administration** of an IgG3 mAb with identical specificity resulted in enhanced pathogenicity in .gamma. chain-deficient and wild-type mice. In vitro studies with isolated macrophages demonstrate that IgG1-, IgG2a-, and IgG2b-opsonized C. neoformans are not phagocytosed or arrested in their growth in the absence of the FcR.gamma. chain. In contrast, opsonization of C. neoformans by IgG3 does not require the presence of the .gamma. chain or of FcRII, and the internalization of IgG3-treated organisms does not arrest fungal growth.

L9 ANSWER 16 OF 26 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 14
ACCESSION NUMBER: 1998:426987 CAPLUS
DOCUMENT NUMBER: 129:131677
TITLE: Effects of granulocyte colony-stimulating factor (G-CSF) treatment on granulocyte function and receptor expression in patients with ventilator-dependent pneumonia
AUTHOR(S): Hustinx, W. N. M.; Van Kessel, C. P. M.; Heezius, E.; Burgers, S.; Lammers, J. -W.; Hoepelman, I. M.
CORPORATE SOURCE: Department of Intensive Care & Clinical Toxicology, Division of Infectious Diseases & AIDS, Utrecht University Hospital, Utrecht, Neth.
SOURCE: Clin. Exp. Immunol. (1998), 112(2), 334-340
CODEN: CEXIAL; ISSN: 0009-9104
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Considerable exptl. evidence in animals suggests that treatment with G-CSF may have a beneficial effect in the management of severe infections in non-neutropenic hosts. This beneficial effect is attributed to an enhancement of granulopoiesis and neutrophil function, the latter possibly involving up-regulation of receptors on neutrophils that are involved in **antibody**-mediated cytotoxicity and killing of microorganisms. We compared neutrophil function and phenotype in blood and bronchoalveolar lavage fluid (BALF) of 10 patients with severe ventilator-dependent pneumonia, at baseline and following initiation of G-CSF treatment as adjunct to std. therapy. G-CSF treatment was assocd. with three-fold increased blood neutrophil counts at day 3 of treatment compared with baseline counts. Mean serum G-CSF concn. increased from 313 to 2007 pg/mL. After correction for lavage diln. effects, BALF G-CSF levels did not differ significantly from baseline, nor did neutrophil receptor expression (**Fc.gamma.RI**, **Fc**. **gamma**.RII, **Fc**.gamma.RIII, CR3, and L-selectin) or indicators of neutrophil function such as respiratory burst activity, phagocytosis and killing of Candida albicans in BALF or blood. The mortality in this group of patients was 30% and compared favorably to the APACHE II-derived predicted mortality of 60%. We conclude that the possible therapeutic benefit of G-CSF **administration** in the early phase of severe bacterial pneumonia is not readily explained by its effect on baseline indicators of neutrophil function or receptor expression.

L9 ANSWER 17 OF 26 MEDLINE DUPLICATE 15
ACCESSION NUMBER: 1999141069 MEDLINE
DOCUMENT NUMBER: 99141069 PubMed ID: 9973640
TITLE: In vivo administration of granulocyte colony-stimulating factor increases the surface expression of sialyl-Lewis(x) on neutrophils in healthy volunteers.
AUTHOR: Ohsaka A; Saionji K
CORPORATE SOURCE: Department of Internal Medicine, Division of Hematology, Hitachi General Hospital, Ibaraki, Japan.. oosaka@cm.nichibyo.hitachi.co.jp
SOURCE: ACTA HAEMATOLOGICA, (1998) 100 (4) 187-90. Journal code: 0S8; 0141053. ISSN: 0001-5792.
PUB. COUNTRY: Switzerland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199904
ENTRY DATE: Entered STN: 19990426
Last Updated on STN: 19990426
Entered Medline: 19990413

AB We examined the in vivo effect of granulocyte colony-stimulating factor (G-CSF) on the surface expression of putative counterligands for endothelial selectins on neutrophils in healthy volunteers. G-CSF (50 microg/m2/day) was **administered** subcutaneously to 5 healthy volunteers for 4 days. The expression of surface antigens on neutrophils was determined by flow cytometry and monoclonal **antibodies**. G-CSF **administration** increased the number of leukocytes, mainly of neutrophils, which was associated with an increase in the expression of the high-affinity Fc receptor for IgG (FcRI, **CD64**) and CD14 on neutrophils. G-CSF **administration** decreased the surface expression of L-selectin on neutrophils, whereas it increased the expression of sialyl-Lewisx but not Lewisx on neutrophils. These findings suggest that G-CSF participates in the neutrophil-endothelial cell interactions in vivo by modulating the expression of adhesion molecules and ligands for endothelial selectins on neutrophils.

L9 ANSWER 18 OF 26 MEDLINE DUPLICATE 16
ACCESSION NUMBER: 1998098165 MEDLINE
DOCUMENT NUMBER: 98098165 PubMed ID: 9435876
TITLE: Clinical experience with CD64-directed immunotherapy. An overview.
AUTHOR: Curnow R T
CORPORATE SOURCE: Medarex Inc., Annadale, NJ 08801, USA.
SOURCE: CANCER IMMUNOLOGY, IMMUNOTHERAPY, (1997 Nov-Dec) 45 (3-4) 210-5. Ref: 9
Journal code: CN3; 8605732. ISSN: 0340-7004.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 19980206
Last Updated on STN: 20000303
Entered Medline: 19980129

AB The class I IgG receptor (**Fc gamma RI** or **CD64** receptor), which is present on key cytotoxic effector cells, has been shown to initiate the destruction of tumor cells in vitro and has been hypothesized to play a role in the destruction of **antibody**-coated cells such as platelets in idiopathic thrombocytopenia purpura (ITP). This overview summarizes the clinical experience with **CD64**-directed immunotherapy in cancer patients with the bispecific **antibodies** MDX-447 [humanized Fab anti-**CD64** x humanized Fab anti-(epidermal growth factor receptor, EGFR)] and MDX-H210 (humanized Fab anti-DC64 x Fab anti-HER2/neu), and with the anti-**CD64** monoclonal **antibody** (mAB) MDX-33 (H22) in the modulation of monocyte **CD64** in vivo. In an ongoing phase I/II open-label trial with progressive dose escalation (1-15 mg/m2), patients with treatment refractory EGFR-positive cancers (renal cell carcinoma (RCC), head and neck, bladder, ovarian, prostate cancer and skin cancer) are treated weekly with intravenous MDX-447, with and without granulocyte-colony-stimulating factor (G-CSF). MDX-447 has been found to be immunologically active at all doses, binding to circulating monocytes and neutrophils (when given with G-CSF), causing monocytopenia and stimulating increases in circulating plasma cytokines. MDX-447 is well tolerated, the primary toxicities being fever, chills, blood pressure lability, and pain/myalgias. Of 36 patients evaluable for response, 9 have experienced stable disease of 3-6 month's duration. The optimal dose and the maximal tolerated dose (MTD) have yet to be defined; dose escalation continues to define better the dose, toxicity, and the potential therapeutic role of this bispecific **antibody**. Three MDX-H210 phase II trials are currently in progress, all using the intravenous dose of 15 mg/m2 given with granulocyte/macrophage (GM-CSF). These consist of one trial each in the treatment of RCC patients, patients with prostate cancer, and colorectal cancer patients, all of whom have failed standard therapy. At the time of writing, 11 patients have been treated in these phase II trials. Four patients have demonstrated antitumor effects. Patients demonstrating responses include 2 with RCC and 2 with prostate cancer. One RCC patient has had a 54% reduction in size of a hepatic metastatic lesion and the other has had a 49% decrease in the size of a lung metastasis with simultaneous clearing of other non-measurable lung lesions. Regarding the two patients with prostate cancer, one has had a 90% reduction in serum prostate-specific antigen (PSA; 118-11 ng/ml), which has persisted for several months; the other patient with prostate has had a 70% reduction of serum PSA (872 ng/ml to 208 ng/ml) within the first month of treatment. Both patients have also demonstrated symptomatic improvement. In a completed phase I and in ongoing phase I/II clinical trials, patients with treatment-refractory HER2/neu positive cancers (breast, ovarian, colorectal, prostate) have been treated with MDX-H210, which has been given alone and in conjunction with G-CSF, GM-CSF, and interferon gamma (IFN gamma). These trials have been open-label, progressive dose-escalation (0.35-135 mg/m2) studies in which single, and more often, multiple weekly doses have been **administered**. MDX-H210 has been well tolerated, with untoward effects being primarily mild-to-moderate flu-like symptoms. The MTD has not yet been defined. MDX-H210 is immunologically active, binding to circulating monocytes, causing monocytopenia, as well as stimulating increases in plasma cytokine levels. Furthermore, some patients have evidence of active antitumor immunity following treatment with MDX-210. Antitumor effects have been seen in response to MDX-H210 **administration**; these include 1 partial, 2 minor, and 1 mixed tumor response; 15 protocol-defined stable disease

responses have occurred. (ABSTRACT TRUNCATED)

L9 ANSWER 19 OF 26 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:23254 CAPLUS
DOCUMENT NUMBER: 128:166120
TITLE: Clinical evaluation of the bispecific antibody MDX-H210 (anti-Fc.gamma.RI .times. antiHER-2/neu) in combination with granulocyte-colony-stimulating factor (Filgrastim) for treatment of advanced breast cancer
AUTHOR(S): Van Ojik, Heidi H.; Repp, Roland; Groenewegen, Gerard; Valerius, Thomas; Van De Winkel, Jan G. J.
CORPORATE SOURCE: Department of Internal Medicine, University Hospital, Utrecht, Neth.
SOURCE: Cancer Immunol. Immunother. (1997), 45(3/4), 207-209
CODEN: CIIMDN; ISSN: 0340-7004
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study sought to define the max. tolerated dose and optimal biol. active dose of of the bispecific **antibody** MDX-H210 in combination with G-CSF, which produces increased nos. of neutrophils with upregulated **Fc.gamma.RI** expression. Breast cancer patients were eligible for this phase I trial if their primary tumor or metastases were overexpressing HER-2/neu. MDX-H20 was **administered** as a 2 h i.v. infusion with an escalating dose in three cohorts and with a fixed dose of Filgrastim s.c. Toxicity was low and manageable, consisting mainly of chills, low-grade fever, nausea and vomiting and pain at metastatic sites. Biol. response was demonstrated by elevated levels of interleukin-6, tumor necrosis factor-.alpha., and G-CSF during the first hours after infusion, increased HER-2/neu levels after infusion, and a decrease in peripheral blood granulocyte and monocyte nos. This study showed that MDX-H210 can be safely **administered** in combination with filgrastim and elicits a biol. response that warrants further clin. evaluation.

L9 ANSWER 20 OF 26 MEDLINE DUPLICATE 17
ACCESSION NUMBER: 96194752 MEDLINE
DOCUMENT NUMBER: 96194752 PubMed ID: 8616043
TITLE: Monoclonal antibody 197 (anti-Fc gamma RI) infusion in a patient with immune thrombocytopenia purpura (ITP) results in down-modulation of Fc gamma RI on circulating monocytes.
AUTHOR: Ericson S G; Coleman K D; Wardwell K; Baker S; Fanger M W; Guyre P M; Ely P
CORPORATE SOURCE: Department of Medicine, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire, USA.
CONTRACT NUMBER: CA-23108 (NCI)
SOURCE: BRITISH JOURNAL OF HAEMATOLOGY, (1996 Mar) 92 (3) 718-24.
Journal code: AXC; 0372544. ISSN: 0007-1048.
PUB. COUNTRY: ENGLAND: United Kingdom
(CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 19960620
Last Updated on STN: 19960620
Entered Medline: 19960610
AB A 44-year old woman with refractory immune thrombocytopenia purpura was treated with the murine monoclonal **antibody** 197 in a phase 1 trial. It vitro studies have demonstrated that the monoclonal **antibody** 197 (subclass IgG2a) binds to two distinct epitopes of **Fc gamma RI**, with the constant domain binding to the Fc-binding portion of the **Fc gamma RI** and the variable domain binding to a different epitope, resulting in crosslinking and modulation of this receptor. The monoclonal **antibody** 197 was **administered** on days 1, 3 and 5 at doses of 0.25 mg/kg, 0.35 mg/kg and 0.45 mg/kg, respectively. The fusions were well tolerated with transient facial flushing, and wheal-and-flare rash during the first infusion, which resolved with a slower infusion rate and the **administration** of diphenhydramine and acetaminophen. Although a marked clinical improvement did occur with resolution of oral ecchymoses and epistaxis after the first mAb infusion, the initial platelet count of 6 x 10(9)/I did not change appreciable over the 5 d course of monoclonal **antibody** treatment. Binding of fluorescein-labelled monoclonal **antibody** 197 to peripheral monocytes showed a rapid and persistently decreased mean fluorescein intensity, indicated binding of **administered** 197 to the monocytes in vivo. Indirect staining for FcgammaRI using fluorescein-labelled goat anti-mouse immunoglobulin was also decreased, suggesting modulation of the receptor. The patient experienced monocytopenia which persisted throughout the 5 d of monoclonal **antibody** 197 therapy, but reversed following institution of intravenous IgG. These data indicate that intravenous monoclonal **antibody** 197 induces specific down-modulation of **Fc gamma RI** expression on monocytes.

L9 ANSWER 21 OF 26 MEDLINE DUPLICATE 18
ACCESSION NUMBER: 95345463 MEDLINE
DOCUMENT NUMBER: 95345463 PubMed ID: 7542496
TITLE: In vitro killing of neuroblastoma cells by neutrophils derived from granulocyte colony-stimulating factor-treated cancer patients using an anti-disialoganglioside/anti-Fc gamma RI bispecific antibody.
AUTHOR: Michon J; Moutel S; Barbet J; Romet-Lemonne J L; Deo Y M; Fridman W H; Teillaud J L
CORPORATE SOURCE: INSERM Unite 255, Institut Curie, Paris, France.
SOURCE: BLOOD, (1995 Aug 1) 86 (3) 1124-30.
Journal code: A8G; 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199508
ENTRY DATE: Entered STN: 19950911
Last Updated on STN: 19960129
Entered Medline: 19950829
AB Neutrophils isolated from cancer patients treated with granulocyte colony-stimulating factor (G-CSF) express high levels of **Fc gamma RI**. They exhibited an efficient killing of GD2+ neuroblastoma cells in the presence of an antidisialoganglioside (GD2) mouse monoclonal **antibody** (MoAb; 7A4, IgG3 kappa). However, this cytotoxicity was totally blocked by human monomeric IgG. In contrast, a

bispecific **antibody** (7A4 bis 22/MDX-260), prepared by chemically linking an F(ab') fragment of 7A4 with an F(ab') fragment of an anti-**Fc gamma RI** MoAb, 22, which binds outside the Fc binding domain, triggered **antibody**-dependent cell cytotoxicity, even when neutrophils were preincubated with human monomeric IgG. F(ab')2 22 MoAb abrogated the MDX-260 killing without affecting that of 7A4. The 3G8 MoAb, directed against the Fc gamma RIII binding site, did not inhibit the cytotoxicity induced by either **antibody**. Thus, these results indicate that G-CSF-activated neutrophils exert their cytotoxic effect against neuroblastoma cells through **Fc gamma RI** and not Fc gamma RIII, and that the saturation of the high affinity **Fc gamma RI** by monomeric IgG can be overcome by the use of bispecific **antibodies** binding epitopes outside the IgG **Fc gamma RI** binding site. A combined **administration** of such bispecific **antibodies** and G-CSF may be, therefore, an efficient therapeutic approach to trigger tumor lysis by cytotoxic neutrophils in vivo.

L9 ANSWER 22 OF 26 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 19
ACCESSION NUMBER: 1995:587882 CAPLUS
DOCUMENT NUMBER: 123:7645
TITLE: In vitro and in vivo effects of rG-CSF on neutrophils
AUTHOR(S): de Haas, M.; Kerst, J. M.; van der Schoot, C. E.; Roos, D.; van Oers, M. H. J.; von dem Borne, A. E. G. Kr.
CORPORATE SOURCE: Central Laboratorium van de Bloedtransfusiedienst, Amsterdam, Neth.
SOURCE: Ned. Tijdschr. Klin. Chem. (1995), 20(2), 82-6
CODEN: NTKCFX; ISSN: 1380-3689
DOCUMENT TYPE: Journal
LANGUAGE: Dutch
AB Granulocyte colony-stimulating factor (G-CSF) stimulates the prodn. of neutrophils and modulates several functions of mature neutrophils. In healthy volunteers the authors studied the effect of a single s.c. dose of rG-CSF (300 .mu.g) on the expression and function of neutrophil Fc.gamma.-receptors (Fc.gamma.R). The authors obsd. that the neutrophils newly formed in response to rG-CSF, were **Fc.gamma. RI** (**CD64**) pos. and were able to perform **antibody** -dependent cellular cytotoxicity. Fc.gamma.RII (CD32) expression was not changed. Expression of the phosphoinositol (PI) linked Fc.gamma.RIII (CD16) was slightly increased immediately after injection and was strongly decreased on the newly formed population. PI-linked CD14 and leukocyte alk. phosphatase showed an increased expression on these cells. The authors found that the initially upregulated expression of Fc.gamma.RIII resulted from rG-CSF induced neutrophil degranulation. Thus, rG-CSF **administration** induces the formation of phenotypically and functionally altered neutrophils.

L9 ANSWER 23 OF 26 MEDLINE DUPLICATE 20
ACCESSION NUMBER: 94342825 MEDLINE
DOCUMENT NUMBER: 94342825 PubMed ID: 8064227
TITLE: Effect of altered CH2-associated carbohydrate structure on the functional properties and in vivo fate of chimeric mouse-human immunoglobulin G1.
AUTHOR: Wright A; Morrison S L
CORPORATE SOURCE: Department of Microbiology and Molecular Genetics, University of California, Los Angeles 90024.
CONTRACT NUMBER: AI-29470 (NIAID)
CA-16858 (NCI)
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1994 Sep 1) 180 (3) 1087-96.
Journal code: I2V; 2985109R. ISSN: 0022-1007.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199409
ENTRY DATE: Entered STN: 19941005
Last Updated on STN: 19941005
Entered Medline: 19940922
AB Immunoglobulin G (IgG) molecules are glycosylated in CH2 at Asn297; the N-linked carbohydrates attached there have been shown to contribute to **antibody** (Ab) stability and various effector functions. The carbohydrate attached to the IgG constant region is a complex biantennary structure. Alterations in the structure of oligosaccharide have been associated with human diseases such as rheumatoid arthritis and osteoarthritis. To study the effects of altered carbohydrate structure on Ab effector function, we have used gene transfection techniques to produce mouse-human chimeric IgG1 Abs in the Chinese hamster ovary (CHO) cell line Lec 1, which is incapable of processing the high-mannose intermediate through the terminal glycosylation steps. We also produced IgG1 Abs in Pro-5, the wild-type CHO cell line that is the parent of Lec 1. The Pro-5-produced Ab (IgG1-Pro-5) was similar to IgG1-My 1, a myeloma-produced IgG1 Ab of the same specificity, in its biologic properties such as serum half-life, ability to effect complement-mediated cytolysis, and affinity for **Fc gamma RI**. Although the Lec 1-produced Ab, IgG1-Lec 1, was properly assembled and retained antigen specificity, it was incapable of complement-mediated hemolysis and was substantially deficient in complement consumption, C1q binding, and C1 activation. IgG1-Lec 1 also showed reduced but significant affinity for **Fc gamma RI** receptors. The in vivo half-life of IgG1-Lec 1 was shorter than that of either the myeloma- or Pro-5-produced counterpart, with more being cleared during the alpha-phase and with more rapid clearance during the beta-phase. Clearance of IgG1-Lec 1 could be inhibited by the **administration** of yeast-derived mannan. Thus the uptake of IgG1-Lec 1 appears to be accelerated by the presence of terminally mannosylated oligosaccharide. Therefore, certain Ab functions as well as the in vivo fate of the protein are dramatically affected by altered carbohydrate structure. Expression of Igs in cell lines with defined glycosylation mutations is shown to be a useful technique for investigating the contribution of carbohydrate structure to Ab function.

L9 ANSWER 24 OF 26 MEDLINE DUPLICATE 21
ACCESSION NUMBER: 93200503 MEDLINE
DOCUMENT NUMBER: 93200503 PubMed ID: 7680917
TITLE: Granulocyte colony-stimulating factor induces hFc gamma RI (CD64 antigen)-positive neutrophils via an effect on myeloid precursor cells.
AUTHOR: Kerst J M; van de Winkel J G; Evans A H; de Haas M; Slaper-Cortenbach I C; de Wit T P; von dem Borne A E; van der Schoot C E; van Oers R H
CORPORATE SOURCE: Central Laboratory of the Red Cross Blood Transfusion

Service, Amsterdam, The Netherlands.
SOURCE: BLOOD, (1993 Mar 15) 81 (6) 1457-64.
Journal code: A8G; 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199304
ENTRY DATE: Entered STN: 19930507
Last Updated on STN: 19960129
Entered Medline: 19930416

AB In this study we have examined hFc gamma RI expression during myelopoiesis. Normal bone marrow (BM) cells were found to express hFc gamma RI up to the metamyelocyte stage. A different **Fc gamma RI** expression pattern was observed in an in vitro model of myelopoiesis. Purified CD34-positive BM cells, cultured for 12 to 14 days with granulocyte colony-stimulating factor (G-CSF), differentiate into a population of mature granulocytic cells. In these cultures, in which hFc gamma RI was virtually absent on the initial CD34-positive BM cells, hFc gamma RI was strongly induced by G-CSF after only 5 days. During final maturation the cells remained hFc gamma RI positive. This expression was confirmed functionally by **antibody**-sensitized erythrocytes (EA)-rosette assays. Moreover, the mature myeloid cells were found to express mRNA encoding for hFc gamma RI, whereas reverse-transcriptase polymerase chain reaction analysis showed that both hFc gamma RIA and hFc gamma RIB genes were expressed. In contrast, on peripheral blood (PB) polymorphonuclear neutrophil leukocytes (PMN) the in vitro effect of G-CSF as to hFc gamma RI induction was limited. Therefore, we conclude that, with respect to hFc gamma RI expression on PMN, G-CSF acts on myeloid precursor cells rather than on mature cells. This conclusion could be strengthened by in vivo **administration** of a single dose of G-CSF to a healthy volunteer. After a 12-hour lag time, hFc gamma RI expressing PMNs were detected in the peripheral blood. This study shows that hFc gamma RI is an early myeloid differentiation marker that is lost during normal final maturation. However, committed myeloid progenitor cells can be strongly induced by G-CSF to express hFc gamma RI, ultimately resulting in mature granulocytic cells expressing the high-affinity receptor for IgG. This expression may have important consequences for the functional capacity of these cells.

L9 ANSWER 25 OF 26 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:406007 CAPLUS
DOCUMENT NUMBER: 117:6007
TITLE: Targeted immunostimulation with bispecific reagents
INVENTOR(S): Romet-Lemonne, Jean Loup; Fanger, Michael W.
PATENT ASSIGNEE(S): Medarex, Inc., USA
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9205793	A1	19920416	WO 1991-US7283	19911004
W: AU, CA, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
CA 2093022	AA	19920406	CA 1991-2093022	19911004
AU 9188694	A1	19920428	AU 1991-88694	19911004
AU 667460	B2	19960328		
EP 553244	A1	19930804	EP 1991-919595	19911004
EP 553244	B1	19981230		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 06502410	T2	19940317	JP 1991-518279	19911004
AT 175118	E	19990115	AT 1991-919595	19911004
ES 2129029	T3	19990601	ES 1991-919595	19911004
US 6248332	B1	20010619	US 1994-249669	19940526
US 6258358	B1	20010710	US 1995-453500	19950530
US 2001048922	A1	20011206	US 2001-899384	20010703

PRIORITY APPLN. INFO.: US 1990-593083 A 19901005
WO 1991-US7283 A 19911004
US 1992-874622 B1 19920427
US 1994-249669 A3 19940526
US 1995-453500 A1 19950530

AB Immune response against an antigen is stimulated by **administering** the antigen in conjunction with a binding agent (e.g. a heteroantibody) specific for an antigen-presenting cell, e.g. a macrophage. The binding agent specifically binds a receptor of the antigen-presenting cell, such as an Fc receptor, without being blocked by the endogenous ligand for the receptor. A bispecific heteroantibody was prepd. from a monoclonal **antibody** against human erythrocytes (mono-D, a human anti-RhD **antibody**) and anti-**Fc.gamma.RI** **antibody** 32 (**Fc.gamma.RI** is the high affinity Fc receptor). The heteroantibody was incubated with erythrocytes, and the heteroantibody-coated erythrocytes were then incubated with adherent monocytes (macrophages). The heteroantibody triggered internalization of the antigen by the macrophages. Enhanced tetanus toxoid presentation by directing tetanus toxoid to human Fc.gamma.R is also described.

L9 ANSWER 26 OF 26 MEDLINE DUPLICATE 22
ACCESSION NUMBER: 91072663 MEDLINE
DOCUMENT NUMBER: 91072663 PubMed ID: 2147695
TITLE: Monocytes and polymorphonuclear neutrophils of patients with streptococcal pharyngitis express increased numbers of type I IgG Fc receptors.
AUTHOR: Guyre P M; Campbell A S; Kniffin W D; Fanger M W
CORPORATE SOURCE: Department of Physiology, Dartmouth Medical School, Hanover, New Hampshire 03756.
CONTRACT NUMBER: AI 19053 (NIAID)
CA 17323 (NCI)
DK 33100 (NIDDK)
+
SOURCE: JOURNAL OF CLINICAL INVESTIGATION, (1990 Dec) 86 (6) 1892-6.
Journal code: HS7; 7802877. ISSN: 0021-9738.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199101
ENTRY DATE: Entered STN: 19910308

Last Updated on STN: 19910308
Entered Medline: 19910122

AB Studies using cultured cells have shown that gamma interferon (IFN-gamma) induces the expression of **Fc gamma RI** (the type I Fc receptor for IgG) on human polymorphonuclear neutrophils (PMN) and greatly increases the number of these receptors on human monocytes. **Administration** of rIFN-gamma in vivo also causes enhanced **Fc gamma RI** expression on these cell populations. Because streptococcal antigens are potent inducers of IFN-gamma in vitro, we postulated that IFN-gamma would be produced endogenously in vivo in patients with streptococcal infections. Such production of IFN-gamma in vivo, even at low levels, might be expected to induce the expression of **Fc gamma RI** on monocytes and neutrophils. To evaluate this possibility, we used monoclonal **antibody** 32 (mAb 32), which is specific for **Fc gamma RI**, to quantitate the expression of this receptor on human peripheral blood cells. We measured the binding of mAb 32 to monocytes and PMNs isolated from healthy donors and from patients with group A beta-hemolytic streptococcal (GABHS) pharyngitis. PMNs from healthy donors (n = 12) had 700 +/- 600 (mean +/- SD) mAb 32 binding sites. Patients with pharyngitis and negative throat culture for GABHS (n = 11) had 2,100 +/- 1,600 sites on their PMNs. In contrast, the PMNs from patients with documented GABHS pharyngitis (n = 12) had 11,600 +/- 7,500 mAb 32 binding sites on their surface. There was a similar change in the expression of **Fc gamma RI** on monocytes, with control monocytes having a mean of 19,900 +/- 3,200 mAb 32 binding sites per cell and the GABHS-positive monocytes having 47,500 +/- 21,400 sites. The GABHS-negative throat culture group had a slightly elevated number of **Fc gamma RI** with a mean of 28,200 +/- 8,400 sites. 10 patients with documented urinary tract infections and three patients with uncomplicated pyelonephritis had no elevation in **Fc gamma RI** expression. These studies demonstrate that a localized group A streptococcal infection can cause systemic activation of the entire circulating pool of phagocytes, and suggest that a similar level of activation is uncommon in localized gram-negative infections of the urinary tract.

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=> s van de Winkel?/au
L10         585 VAN DE WINKEL?/AU

=> s l10 and macrophage? or CD64
L11        1074 L10 AND MACROPHAGE? OR CD64

=> s l10 and (macrophage? or CD64)
L12         183 L10 AND (MACROPHAGE? OR CD64)

=> s l12 (P) antibod?
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L42 (P) ANTIBOD?'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L43 (P) ANTIBOD?'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L44 (P) ANTIBOD?'
L13         127 L12 (P) ANTIBOD?

=> s l13 (P) administ?
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L46 (P) ADMINIST?'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L47 (P) ADMINIST?'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L48 (P) ADMINIST?'
L14          11 L13 (P) ADMINIST?

=> dup rem l14
PROCESSING COMPLETED FOR L14
L15            7 DUP REM L14 (4 DUPLICATES REMOVED)

=> dis l151-7 ibib abs
'L999-28' IS NOT A VALID FORMAT
In a multifile environment, a format can only be used if it is valid
in at least one of the files.  Refer to file specific help messages
or the STNGUIDE file for information on formats available in
individual files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):end

=> dis l15 1-7 ibib abs

L15  ANSWER 1 OF 7      MEDLINE
ACCESSION NUMBER:    2001320055      MEDLINE
DOCUMENT NUMBER:     21286444   PubMed ID: 11390445
TITLE:               Neutrophil Fc gamma RI as target for immunotherapy of
                     invasive candidiasis.
AUTHOR:              van Spriel A B; van den Herik-Oudijk I E; van de
                     Winkel J G
CORPORATE SOURCE:    Immunotherapy Laboratory, Medarex Europe, and Genmab,
                     University Medical Center, Utrecht, The Netherlands.
SOURCE:              JOURNAL OF IMMUNOLOGY, (2001 Jun 15) 166 (12) 7019-22.
                     Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY:        United States
                     Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH:         200108
ENTRY DATE:          Entered STN: 20010827
                     Last Updated on STN: 20010827
                     Entered Medline: 20010823
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AB Invasive candidiasis represents a life-threatening disease for immunocompromised patients. This study focused on new immunotherapeutic approaches for systemic Candida albicans infections in a human FcgammaRI-transgenic mouse model. FcgammaRI (**CD64**) is a potent immunoactivating receptor on phagocytic and dendritic cells. In vivo targeting of C. albicans toward neutrophil-FcgammaRI by bispecific Abs and G-CSF effectively protected FcgammaRI-transgenic mice from lethal candidiasis. Nontransgenic mice were not protected, and treatment with bispecific Ab or G-CSF alone did not reduce mortality. Furthermore, infected FcgammaRI-transgenic mice developed high titers of anti-C. albicans IgG, and survival was extended on secondary infection without further treatment. These findings document the capacity of FcgammaRI to initiate potent anti-C. albicans immunity and support the development of FcgammaRI-directed immunotherapy of invasive fungal disease.

L15 ANSWER 2 OF 7 MEDLINE
ACCESSION NUMBER: 2001091107 MEDLINE
DOCUMENT NUMBER: 20570905 PubMed ID: 11120792
TITLE: Targeting weak antigens to **CD64** elicits potent humoral responses in human **CD64** transgenic mice.
AUTHOR: Keler T; Guyre P M; Vitale L A; Sundarapandiyan K; **van De Winkel J G**; Deo Y M; Graziano R F
CORPORATE SOURCE: Medarex, Inc., Annandale, NJ 08801, USA..
tkeler@injersey.com
SOURCE: JOURNAL OF IMMUNOLOGY, (2000 Dec 15) 165 (12) 6738-42.
Journal code: IFB. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010125

AB Previous studies have documented that targeting foreign Ags to IgG FcgammaR leads to enhanced Ag-specific responses in vitro and in vivo. However, the ability to overcome immunologic nonresponsiveness by targeting poorly immunogenic Ags to FcgammaR has not been investigated. To address this question in a simple model, we immunized transgenic mice expressing human **CD64** (FcgammaRI) and their nontransgenic littermates with Fab' derived from the murine anti-human **CD64** mAb m22. The m22 Fab' served as both the targeting molecule and the Ag. We found that only **CD64**-expressing mice developed anti-Id titers to m22. Furthermore, chemically linked multimers of m22 Fab', which mediated efficient internalization of the human **CD64**, were significantly more potent than monomeric m22 F(ab')(2) at inducing anti-Id responses. In all cases, the humoral responses were specific for m22 Id and did not react with other murine IgG1 Fab' fragments. Chemical addition of a second murine Fab' (520C9 anti-human HER2/neu) to m22 Fab' multimers demonstrated that IgG1 and IgG2a anti-Id titers could be generated to 520C9 only in the **CD64**-expressing mice. These results show that targeting to **CD64** can overcome immunological nonresponsiveness to a weak immunogen. Therefore, targeting to **CD64** may be an effective method to enhance the activity of nonimmunogenic tumor vaccines.

L15 ANSWER 3 OF 7 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2000091141 MEDLINE
DOCUMENT NUMBER: 20091141 PubMed ID: 10625390
TITLE: Resolution of cutaneous inflammation after local elimination of **macrophages**.
COMMENT: Comment in: Nat Biotechnol. 2000 Jan;18(1):25-6
AUTHOR: Thepen T; van Vuuren A J; Kiekens R C; Damen C A; Vooijs W C; **van De Winkel J G**
CORPORATE SOURCE: Department of Immunology, University Medical Center Utrecht, Utrecht, The Netherlands.
SOURCE: NATURE BIOTECHNOLOGY, (2000 Jan) 18 (1) 48-51.
Journal code: CQ3; 9604648. ISSN: 1087-0156.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000314
Last Updated on STN: 20000314
Entered Medline: 20000229

AB We constructed an immunotoxin, composed of an **antibody** directed against the high-affinity IgG receptor **CD64** and Ricin-A, with the aim of resolving chronic inflammation through elimination of activated **macrophages**. In vitro, this immunotoxin proved very efficient in inducing apoptosis in activated **macrophages**, leaving resting and low **CD64**-expressing **macrophages** unaffected. We examined the activity of our immunotoxin in a sodium lauryl sulfate (SLS)-induced cutaneous inflammation model, using transgenic mice expressing human **CD64**. Upon intradermal injection of the immunotoxin (IT), cutaneous inflammation resolved in 24 h. This was demonstrated histologically by clearance of all **CD64**-expressing **macrophages**, followed by clearance of other inflammatory cells. Clinical parameters associated with inflammation, such as local skin temperature and vasodilation, also decreased.

L15 ANSWER 4 OF 7 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 1998208286 MEDLINE
DOCUMENT NUMBER: 98208286 PubMed ID: 9548506
TITLE: Generation of HER-2/neu-specific cytotoxic neutrophils in vivo: efficient arming of neutrophils by combined **administration** of granulocyte colony-stimulating factor and Fcgamma receptor I bispecific **antibodies**.
AUTHOR: Heijnen I A; Rijks L J; Schiel A; Stockmeyer B; van Ojik H H; Dechant M; Valerius T; Keler T; Tutt A L; Glennie M J; van Royen E A; Capel P J; **van de Winkel J G**
CORPORATE SOURCE: Department of Immunology, University Hospital Utrecht, The Netherlands.
SOURCE: JOURNAL OF IMMUNOLOGY, (1997 Dec 1) 159 (11) 5629-39.
Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199804
ENTRY DATE: Entered STN: 19980430
Last Updated on STN: 20000303
Entered Medline: 19980420

AB Abs are able to induce inflammatory antitumor responses by recruiting IgG Fc receptor (FcgammaR)-bearing cytotoxic effector cells. We recently described the capacity of the high affinity FcgammaRI (**CD64**) to trigger cytotoxic activity of neutrophils (PMN) during granulocyte CSF (G-CSF) treatment. To take advantage of FcgammaRI as a cytotoxic trigger molecule on PMN, two Ab constructs were prepared. We show that a chimeric human IgG1 Ab (Ch520C9) and an anti-FcgammaRI bispecific Ab (BsAb; 22x520C9), both directed to the proto-oncogene product HER-2/neu, interact with FcgammaRI. In addition, both Ab constructs mediate enhanced lysis of HER-2/neu-expressing tumor cells by G-CSF-primed PMN. However, engagement of FcgammaRI by Ch520C9 was inhibited by human serum IgG, thereby abrogating the enhanced Ch520C9-mediated cytotoxicity. BsAb 22x520C9, which binds FcgammaRI outside the ligand binding domain, effectively recruits the cytotoxic potential of FcgammaRI on G-CSF-primed PMN regardless of the presence of human serum. These results indicate that

under physiologic conditions, serum IgG impairs activation of FcgammaRI-mediated cytotoxicity by conventional antitumor Abs. The IgG blockade can be circumvented with anti-FcgammaRI BsAbs. Using human FcgammaRI transgenic mice we demonstrate that BsAb 22x520C9 is able to engage FcgammaRI in vivo. BsAb 22x520C9 injected i.v. was readily detected on circulating PMN of G-CSF-treated transgenic animals. In addition, we showed that PMN remain "armed" with BsAb 22x520C9 during migration to inflammatory sites, and that after isolation such PMN specifically lyse HER-2/neu-expressing tumor cells. These results point to the possibility of targeting anti-FcgammaRI BsAbs to G-CSF-primed PMN in vivo, endowing them with specific anti-tumor activity.

L15 ANSWER 5 OF 7 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96037950 EMBASE
DOCUMENT NUMBER: 1996037950
TITLE: Antigen targeting to myeloid-specific human Fc.gamma.RI/ **CD64** triggers enhanced **antibody** responses in transgenic mice.
AUTHOR: Heijnen I.A.F.M.; Van Vugt M.J.; Fanger N.A.; Graziano R.P.; De Wit T.P.M.; Hofhuis F.M.A.; Guyre P.M.; Capel P.J.A.; Verbeek J.S.; **Van de Winkel J.G.J.**
CORPORATE SOURCE: Department of Immunology, University Hospital Utrecht, Heidelberglaan 100,3584 CX Utrecht, Netherlands
SOURCE: Journal of Clinical Investigation, (1996) 97/2 (331-338). ISSN: 0021-9738 CODEN: JCINAO
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Besides their phagocytic effector functions, myeloid cells have an essential role as accessory cells in the induction of optimal humoral immune responses by presenting captured antigens and activating lymphocytes. Antigen presentation by human monocytes was recently found to be enhanced in vitro through the high-affinity Fc receptor for IgG (Fc.gamma.RI; **CD64**), which is exclusively present on myeloid cells. To evaluate a comparable role of Fc.gamma.RI in antigen presentation in vivo, we generated human Fc.gamma.RI transgenic mice. Under control of its endogenous promoter, human Fc.gamma.RI was selectively expressed on murine myeloid cells at physiological expression levels. As in humans, expression was properly regulated by the cytokines IFN-.gamma., G-CSF, IL-4, and IL-10, and was up- regulated during inflammation. The human receptor expressed by murine **macrophages** bound monomeric human IgG and mediated particle phagocytosis and IgG complex internalization. To evaluate whether specific targeting of antigens to Fc.gamma.RI can induce enhanced **antibody** responses, mice were immunized with an antihuman Fc.gamma.RI **antibody** containing antigenic determinants. Transgenic mice produced antigen-specific **antibody** responses with high IgG1 titers and substantial IgG2a and IgG2b responses. These data demonstrate that human Fc.gamma.RI on myeloid cells is highly active in mediating enhanced antigen presentation in vivo, and show that anti-Fc.gamma.RI mAbs are promising vaccine adjuvants.

L15 ANSWER 6 OF 7 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95336576 EMBASE
DOCUMENT NUMBER: 1995336576
TITLE: G-CSF-stimulated PMN in immunotherapy of breast cancer with a bispecific **antibody** to Fc.gamma.RI and to HER-2/neu (MDX-210).
AUTHOR: Repp R.; Valerius T.; Wieland G.; Becker W.; Steininger H.; Deo Y.; Helm G.; Gramatzki M.; **Van de Winkel J.G.J.** ; Lang N.; Kalden J.R.
CORPORATE SOURCE: Division of Hematology/Oncology, Department of Medicine III, University of Erlangen-Nurnberg, Krankenhausstrasse 12,8520 Erlangen, Germany
SOURCE: Journal of Hematotherapy, (1995) 4/5 (415-421). ISSN: 1061-6128 CODEN: JOEMEL
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 016 Cancer
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Myeloid cells can mediate tumor cell cytotoxicity via certain receptors for immunoglobulins. Among the different Fc receptors, the high-affinity IgG receptor (Fc.gamma.RI, **CD64**) is a promising trigger molecule because it is selectively expressed on effector cells, including monocytes/**macrophages** and granulocyte colony-stimulating factor (G-CSF)-primed neutrophils. In vitro, a bispecific **antibody** (BsAb) (MDX-210, constructed by chemically cross-linking F(ab') fragments of monoclonal **antibody** (mAb) 520C9 to HER-2/neu and F(ab') fragments of mAb 22 to Fc.gamma.RI) mediated effective lysis of HER-2/neu overexpressing breast cancer cell lines. HER-2/neu (c-erbB2) is overexpressed in approximately 30% of breast and ovarian carcinomas and is a target for immunotherapy in clinical trials. In vitro assays showed Fc.gamma.RI-positive neutrophils to constitute a major effector cell population during G-CSF therapy. Based on these preclinical data and a preceding study at Dartmouth (New Hampshire) with a single dose of MDX-210 alone, a combination of G-CSF and MDX-210 is tested in a phase I study in breast cancer patients. In this study, patients receiving G-CSF are treated with escalating single doses of MDX-210. This therapy was generally well tolerated by the treated patients, some of whom reacted with fever and short periods of chills, which were temporally related to elevated plasma levels of IL-6 and TNF-.alpha.. After MDX- 210 application, a transient decrease in the total white blood count and absolute neutrophil count (ANC) was observed. During G-CSF application, isolated neutrophils were highly cytotoxic in the presence of MDX-210 in vitro. These data indicate a potential role for G-CSF and BsAb in immunotherapy.

L15 ANSWER 7 OF 7 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 93200503 MEDLINE
DOCUMENT NUMBER: 93200503 PubMed ID: 7680917
TITLE: Granulocyte colony-stimulating factor induces hFc gamma RI (**CD64** antigen)-positive neutrophils via an effect on myeloid precursor cells.
AUTHOR: Kerst J M; **van de Winkel J G**; Evans A H; de Haas M; Slaper-Cortenbach I C; de Wit T P; von dem Borne A E; van der Schoot C E; van Oers R H

CORPORATE SOURCE: Central Laboratory of the Red Cross Blood Transfusion Service, Amsterdam, The Netherlands.
SOURCE: BLOOD, (1993 Mar 15) 81 (6) 1457-64.
Journal code: A8G; 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199304
ENTRY DATE: Entered STN: 19930507
Last Updated on STN: 19960129
Entered Medline: 19930416

AB In this study we have examined hFc gamma RI expression during myelopoiesis. Normal bone marrow (BM) cells were found to express hFc gamma RI up to the metamyelocyte stage. A different Fc gamma RI expression pattern was observed in an in vitro model of myelopoiesis. Purified CD34-positive BM cells, cultured for 12 to 14 days with granulocyte colony-stimulating factor (G-CSF), differentiate into a population of mature granulocytic cells. In these cultures, in which hFc gamma RI was virtually absent on the initial CD34-positive BM cells, hFc gamma RI was strongly induced by G-CSF after only 5 days. During final maturation the cells remained hFc gamma RI positive. This expression was confirmed functionally by **antibody**-sensitized erythrocytes (EA)-rosette assays. Moreover, the mature myeloid cells were found to express mRNA encoding for hFc gamma RI, whereas reverse-transcriptase polymerase chain reaction analysis showed that both hFc gamma RIA and hFc gamma RIB genes were expressed. In contrast, on peripheral blood (PB) polymorphonuclear neutrophil leukocytes (PMN) the in vitro effect of G-CSF as to hFc gamma RI induction was limited. Therefore, we conclude that, with respect to hFc gamma RI expression on PMN, G-CSF acts on myeloid precursor cells rather than on mature cells. This conclusion could be strengthened by in vivo **administration** of a single dose of G-CSF to a healthy volunteer. After a 12-hour lag time, hFc gamma RI expressing PMNs were detected in the peripheral blood. This study shows that hFc gamma RI is an early myeloid differentiation marker that is lost during normal final maturation. However, committed myeloid progenitor cells can be strongly induced by G-CSF to express hFc gamma RI, ultimately resulting in mature granulocytic cells expressing the high-affinity receptor for IgG. This expression may have important consequences for the functional capacity of these cells.

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=> dis his

     (FILE 'HOME' ENTERED AT 09:36:34 ON 05 APR 2002)

     FILE 'MEDLINE, CAPLUS, EMBASE' ENTERED AT 09:36:54 ON 05 APR 2002
L1             7 S FCGAMMAR1
L2            65 S FC (1N) GAMMA (1N) R1
L3          1957 S FC (1N) GAMMA (1N) RI
L4           982 S CD64
L5             0 S L1 AND L2 AND L3 AND L4
L6          2547 S L1 OR L2 OR L3 OR L4
L7          1130 S L6 (P) ANTIBOD?
L8            54 S L7 (P) ADMINIST?
L9            26 DUP REM L8 (28 DUPLICATES REMOVED)
L10          585 S VAN DE WINKEL?/AU
L11         1074 S L10 AND MACROPHAGE? OR CD64
L12          183 S L10 AND (MACROPHAGE? OR CD64)
L13          127 S L12 (P) ANTIBOD?
L14           11 S L13 (P) ADMINIST?
L15            7 DUP REM L14 (4 DUPLICATES REMOVED)

=> s l4 (P) macrophage?
L16          299 L4 (P) MACROPHAGE?

=> s l16 and psoriasis
L17            0 L16 AND PSORIASIS

=> s l16 and (hiv)
L18           10 L16 AND (HIV)

=> dup rem l18
PROCESSING COMPLETED FOR L18
L19            5 DUP REM L18 (5 DUPLICATES REMOVED)

=> dis l19 1-5 ibib abs

L19  ANSWER 1 OF 5     MEDLINE                              DUPLICATE 1
ACCESSION NUMBER:   2001364831     MEDLINE
DOCUMENT NUMBER:    21318629   PubMed ID: 11426066
TITLE:              Increased priming for interleukin-12 and tumour necrosis
                    factor alpha in CD64 monocytes in HIV infection:
                    modulation by cytokines and therapy.
AUTHOR:             Bocchino M; Ledru E; Debord T; Gougeon M L
CORPORATE SOURCE:   Departement SIDA et Retrovirus, Institut Pasteur, Hopital
                    Begin, Paris, France.
SOURCE:             AIDS, (2001 Jul 6) 15 (10) 1213-23.
                    Journal code: AID; 8710219. ISSN: 0269-9370.
PUB. COUNTRY:       England: United Kingdom
                    Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200108
ENTRY DATE:         Entered STN: 20010813
                    Last Updated on STN: 20010813
                    Entered Medline: 20010809
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AB BACKGROUND: A key factor leading to impaired immunity in **HIV** infection is an alteration of the pattern of cytokine response, although its precise nature remains controversial, particularly the in vivo influence of **HIV** on interleukin (IL)-12 synthesis. DESIGN: A cross-sectional study in 73 **HIV**-infected persons (28 of them receiving highly active antiretroviral therapy) and 18 **HIV** -seronegative healthy donors. METHODS: The frequency of monocytes/ **macrophages** (M/M) synthesizing IL-12, IL-10 and tumour necrosis factor alpha (TNF-alpha) was determined in peripheral blood mononuclear cells. The cells were cultured in medium or were stimulated with lipopolysaccharide; proportions of **CD64** M/M producing IL-12, TNF-alpha or IL-10 was determined by cytofluorometric analysis. The influence of exogenous interferon gamma (IFN-gamma), IL-10 or IL-15 on IL-12 synthesis was tested. RESULTS: Chronic **HIV** disease is associated with increased priming of M/M for IL-12 (involving both p40 and p70 molecules) and TNF-alpha synthesis; this was associated with

cosynthesis of both cytokines by a fraction of M/M. Priming for IL-12 was physiologically enhanced by IFN-gamma and decreased by IL-10; IL-15 had no effect. The proportion of IL-10-producing **CD64** M/M was not altered in patients compared with controls but there was an inverse correlation between IL-10-producing M/M and viral load. IL-12 production was not correlated with viral load but was increased following antiretroviral therapy. Following LPS stimulation, IL-12 and TNF-alpha responses were not altered in **HIV**-positive patients; however, the IL-10 response was decreased but restored by antiretroviral therapy. CONCLUSION: These observations argue for a preserved intrinsic **CD64** M/M of IL-12 production in **HIV** pathogenesis.

L19 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:908511 CAPLUS
DOCUMENT NUMBER: 135:44922
TITLE: Targeting **HIV**-1 gp120 to the high affinity FC receptor (FC.gamma.RI, CD64) on myeloid antigen presenting cells: implications for enhancing vaccine responses
AUTHOR(S): Howell, Alexandra L.; Thacker, Tara N.; Li, Fang; Fiering, Steve; Graziano, Robert F.; Goldstein, Joel; Fanger, Michael W.
CORPORATE SOURCE: V.A. Medical Center, VT, 05009, USA
SOURCE: Current Topics in Virology (1999), 1, 61-70
CODEN: CTVUAG
PUBLISHER: Research Trends
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We prepd. a fusion protein contg. a humanized monoclonal antibody (mAb), mAb H22, with specificity for the human high affinity Fc receptor for IgG (Fc.gamma.RI, **CD64**), fused to **HIV**-1 gp120. This fusion protein construct was produced by joining the cDNA for the full length H22 heavy chain gene in frame to the cDNA for gp120. This construct, which also expressed a selectable marker, was stably transfected into a murine myeloma cell line that expressed the previously transfected H22 kappa light chain. The resulting fusion protein, (H22 .times. gp120), was secreted from the myeloma cell line and was purified by affinity chromatog. Flow cytometric anal. revealed that H22 .times. gp120 bound with high affinity via the Fab portion of H22 to **CD64** expressed on monocytes and **macrophages** from both humans and human **CD64**-expressing transgenic mice. Western blot anal. revealed that the 390 kDa fusion protein reacted with both anti-human IgG and anti-gp120 mAbs. Incubation of a monocyte cell line with this fusion protein at 37.degree.C resulted in internalization of the complex as detd. by flow cytometric anal. Immunization of human **CD64** transgenic mice with the purified H22 .times. gp120 fusion protein induced higher titers of anti-gp120 serum antibodies compared to immunization of non-transgenic littermates. Targeting gp120 to **CD64**-expressing antigen presenting cells (APC) in vivo may augment immune responses and enhance protective immunity.
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 3 OF 5 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 97163433 MEDLINE
DOCUMENT NUMBER: 97163433 PubMed ID: 9010253
TITLE: Progression of **HIV** disease is associated with increased expression of Fc gammaRI and CR1 on alveolar macrophages.
AUTHOR: Gilbody J; Lipman M C; Johnson M A; Atkins M; Poulter L W
CORPORATE SOURCE: Department of Clinical Immunology, Royal Free Hospital and School of Medicine, London, UK.
SOURCE: CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (1997 Jan) 107 (1) 31-6.
Journal code: DD7; 0057202. ISSN: 0009-9104.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970306
Last Updated on STN: 19970306
Entered Medline: 19970221
AB The expression of receptors for complement and the Fc region of immunoglobulin by alveolar **macrophages** (AM) constitutes a valuable aid to effector function of these cells. However, during **HIV** infection such expression may also act to increase binding of immune complexes, thus facilitating viral infection of these cells. This study was designed to determine whether changes in the expression of these receptors occurs in situ during **HIV** infection. Lung **macrophages** were isolated by bronchoalveolar lavage in groups of **HIV**+ subjects segregated on the basis of peripheral CD4 count. A group of normal subjects was also investigated. Expression of CR1 and Fc gammaRI was quantified by measuring the optical density of reaction product following controlled immunoperoxidase staining with MoAbs CD35 and **CD64**. Both CR1 and Fc gammaRI were increased over normal in all **HIV**+ subjects. This increase was progressive with advancing disease as determined by correlation with declining peripheral CD4 count. Comparison of asymptomatic and symptomatic subjects with **HIV** infection showed no difference in CR1 expression but a rise in Fc gammaRI expression in the latter group. An overall inverse correlation was also found between peripheral CD4 count and Fc gammaRI expression, but not CR1 expression. These data demonstrate a significant increase in the expression of these receptors on AM from **HIV**+ subjects, and show that this increase may occur before any symptoms in these patients.

L19 ANSWER 4 OF 5 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 92229078 MEDLINE
DOCUMENT NUMBER: 92229078 PubMed ID: 1533048
TITLE: Functional consequences of monocyte/macrophage infection by HIV1.
AUTHOR: Le Naour R; Raoul H; Mabondzo A; Ripoll L; Bartholeyns J; Romet-Lemonne J L; Dormont D
CORPORATE SOURCE: Laboratoire de Neuropathologie experimentale et Neurovirologie, Commissariat a l'Energie Atomique, CRSSA/DSV/DPTE, Fontenay-aux-Roses, France.
SOURCE: RESEARCH IN IMMUNOLOGY, (1992 Jan) 143 (1) 49-56.
Journal code: R6E; 8907467. ISSN: 0923-2494.
PUB. COUNTRY: France
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199205

ENTRY DATE: Entered STN: 19920607
Last Updated on STN: 19970203
Entered Medline: 19920519

AB Monocyte/**macrophage** infection by human immunodeficiency virus type 1 (HIV1) was studied for its effects on the production of tumour necrosis factor alpha (TNF alpha) and the expression of the manganese superoxide dismutase (MnSOD) gene. For this purpose, human peripheral blood monocytes were obtained from healthy HIV1-seronegative donors by centrifugal elutriation and infected with either the HIV1/LAV1 strain or with the primary HIV1/DAS isolate. The results showed that (1) HIV1/LAV1-infected **macrophages** did not produce any biologically detectable TNF alpha during the few hours following lentiviral infection, despite rises in the TNF alpha mRNA level; (2) MnSOD gene transcription in the **macrophages** increased, as measured 2 and 4 h after infection; (3) the level of the MnSOD gene expression declined during the late phases of lentiviral infection, but TNF alpha synthesis and gene expression rose; and (4) bispecific antibody comprised of anti-Fc gamma RI (anti-**CD64**) and anti-gp41 monoclonal antibodies inhibited the in vitro infection of monocyte-derived **macrophages** by HIV1/DAS.

L19 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:677836 CAPLUS
DOCUMENT NUMBER: 115:277836
TITLE: Fc receptors for IgG (Fc.gamma.Rs) on human monocytes and macrophages are not infectivity receptors for human immunodeficiency virus type 1 (**HIV**-1): studies using bispecific antibodies to target **HIV**-1 to various myeloid cell surface molecules, including the Fc.gamma.R
AUTHOR(S): Connor, R. I.; Dinces, N. B.; Howell, A. L.; Romet-Lemonne, J. L.; Pasquali, J. L.; Fanger, M. W.
CORPORATE SOURCE: Dep. Microbiol., Dartmouth Med. Sch., Hanover, NH, 03756, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1991), 88(21), 9593-7
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Fc.gamma.Rs (Fc.gamma.RI, Fc.gamma.RII, and Fc.gamma.RIII) are highly expressed on human mononuclear phagocytes and function in the clearance of immune complexes and opsonized pathogens. The authors examd. the role of Fc.gamma.R in mediating antibody-dependent clearance of **HIV**-1 by human monocytes and monocyte-derived macrophages by using bispecific antibodies (BsAbs) to independently target the virus to Fc.gamma.RI, Fc.gamma.RII, or Fc.gamma.RIII. Virus prodn. was markedly reduced in monocytes cultured with strain **HIV**-1IIIB opsonized with BsAbs that target the virus to either Fc.gamma.RI or Fc.gamma.RII compared to monocytes cultured with virus in the absence of BsAbs or in the presence of BsAbs that target the virus to non-Fc.gamma.R surface antigens (CD33 and HLA-A,B,C). These results were confirmed using the monotropic isolate **HIV**-1JRFL. Interaction of **HIV**-1JRFL with Fc.gamma.RII on human monocytes and Fc.gamma.RI, Fc.gamma.RII, or Fc.gamma.RIII on monocyte-derived macrophages resulted in markedly reduced levels of virus prodn. in these cultures. Moreover, **HIV**-1 infection of monocytes and monocyte-derived macrophages was completely blocked by anti-CD4 monoclonal antibodies, indicating that interaction with CD4 is required for infectivity even under conditions of antibody-mediated binding of **HIV**-1 to Fc.gamma.R. Thus, it is proposed that highly opsonized **HIV**-1 initiates high-affinity multivalent interactions with Fc.gamma.R that trigger endocytosis and intracellular degrdn. of the antibody-virus complex. At lower levels of antibody opsonization, there are too few interactions with Fc.gamma.R to initiate endocytosis and intracellular degrdn. of the antibody-virus complex, but there are enough interactions to stabilize the virus at the cell surface, allowing antibody-dependent enhancement of **HIV**-1 infection through high-affinity CD4 interactions. However, interaction of highly opsonized **HIV**-1 with Fc.gamma.Rs through BsAbs may reduce viral infectivity through Fc.gamma.R-mediated cytotoxic mechanisms and, therefore, BsAbs offer promise as therapeutic reagents in **HIV**-1 infections.

=> s l16 and (lupus or scleroderma or dermatitis or wegener? or RA or MS)
L20 23 L16 AND (LUPUS OR SCLERODERMA OR DERMATITIS OR WEGENER? OR RA OR MS)

=> dup rem l20
PROCESSING COMPLETED FOR L20
L21 12 DUP REM L20 (11 DUPLICATES REMOVED)

=> dis l21 1-12 ibib abs

L21 ANSWER 1 OF 12 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2000408999 MEDLINE
DOCUMENT NUMBER: 20307315 PubMed ID: 10848732
TITLE: Expression of Fc receptors for IgG during acute and chronic cutaneous inflammation in atopic **dermatitis**.
AUTHOR: Kiekens R C; Thepen T; Bihari I C; Knol E F; Van De Winkel J G; Bruijnzeel-Koomen C A
CORPORATE SOURCE: Departments of Dermatology/Allergology G02.124 and Immunology, and Medarex Europe, University Medical Center Utrecht, Heidelberglaan 100, 3584 CX Utrecht, The Netherlands.
SOURCE: BRITISH JOURNAL OF DERMATOLOGY, (2000 Jun) 142 (6) 1106-13.
Journal code: AW0; 0004041. ISSN: 0007-0963.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000907
Last Updated on STN: 20000907
Entered Medline: 20000831

AB Atopic **dermatitis** is an allergic skin disease characterized by elevated total and antigen-specific serum IgE and IgG4 levels. In acute and chronic cutaneous inflammation, large cellular infiltrates including T cells, dendritic cells and **macrophages** are found, especially in the dermis. These cells play an important part in the regulation of local inflammatory reactions. Receptors binding IgG (FcgammaR) are involved in dendritic cell and **macrophage** function. In this study, we examined the in vivo distribution and cellular expression of the three classes of leucocyte FcgammaR in human skin during acute and chronic cutaneous inflammation in atopic **dermatitis**. Atopy patch test skin was used as a model for acute inflammation in atopic

dermatitis, while chronic lesional skin was used to investigate FcgammaR expression in chronically inflamed skin. In atopy patch test sites no increase in the number of CD1a+ dendritic cells and a slight increase in **macrophages** compared with non-lesional skin was observed. Our results showed increased expression of FcgammaRI (**CD64**) and FcgammaRIII (CD16) in acutely inflamed skin as well as in chronically inflamed lesional skin, compared with healthy and non-lesional atopic **dermatitis** skin. FcgammaRI was expressed by RFD1+, RFD7+ and CD68+, but not by CD1a+ dermal dendritic cells. RFD1+ dendritic cells and CD68+ **macrophages** were the main FcgammaRIII-expressing cells during the acute inflammatory reaction. The significant increase in expression of FcgammaRIII (CD16) and FcgammaRI (**CD64**) probably results from upregulation of the receptors on resident cells. Insight into the presence of FcgammaR+ cells in human skin during inflammation is important both for our understanding of skin immune reactions and the development of new therapeutic concepts.

L21 ANSWER 2 OF 12 MEDLINE
ACCESSION NUMBER: 2000091141 MEDLINE
DOCUMENT NUMBER: 20091141 PubMed ID: 10625390
TITLE: Resolution of cutaneous inflammation after local elimination of macrophages.
COMMENT: Comment in: Nat Biotechnol. 2000 Jan;18(1):25-6
AUTHOR: Thepen T; van Vuuren A J; Kiekens R C; Damen C A; Vooijs W C; van De Winkel J G
CORPORATE SOURCE: Department of Immunology, University Medical Center Utrecht, Utrecht, The Netherlands.
SOURCE: NATURE BIOTECHNOLOGY, (2000 Jan) 18 (1) 48-51. Journal code: CQ3; 9604648. ISSN: 1087-0156.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000314
Last Updated on STN: 20000314
Entered Medline: 20000229

AB We constructed an immunotoxin, composed of an antibody directed against the high-affinity IgG receptor **CD64** and Ricin-A, with the aim of resolving chronic inflammation through elimination of activated **macrophages**. In vitro, this immunotoxin proved very efficient in inducing apoptosis in activated **macrophages**, leaving resting and low **CD64**-expressing **macrophages** unaffected. We examined the activity of our immunotoxin in a sodium lauryl sulfate (SLS)-induced cutaneous inflammation model, using transgenic mice expressing human **CD64**. Upon intradermal injection of the immunotoxin (IT), cutaneous inflammation resolved in 24 h. This was demonstrated histologically by clearance of all **CD64**-expressing **macrophages**, followed by clearance of other inflammatory cells. Clinical parameters associated with inflammation, such as local skin temperature and vasodilation, also decreased.

L21 ANSWER 3 OF 12 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 1999293237 MEDLINE
DOCUMENT NUMBER: 99293237 PubMed ID: 10364903
TITLE: Monocyte activation in patients with **Wegener**'s granulomatosis.
AUTHOR: Muller Kobold A C; Kallenberg C G; Tervaert J W
CORPORATE SOURCE: Department of Clinical Immunology, University Hospital Groningen, The Netherlands.
SOURCE: ANNALS OF THE RHEUMATIC DISEASES, (1999 Apr) 58 (4) 237-45. Journal code: 62W; 0372355. ISSN: 0003-4967.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990712
Last Updated on STN: 20000303
Entered Medline: 19990621

AB OBJECTIVE: **Wegener**'s granulomatosis (WG) is an inflammatory disorder characterised by granulomatous inflammation, vasculitis, and necrotising vasculitis and is strongly associated with anti-neutrophil cytoplasmic antibodies (ANCA). Activated monocytes/**macrophages** are present in renal biopsy specimens and participate in granuloma formation by synthesising and secreting a variety of chemoattractants, growth factors, and cytokines. In view of these findings, in vivo monocyte activation was evaluated in patients with WG and the findings related to parameters of clinical disease activity. METHODS: Monocyte activation was analysed by measuring plasma concentrations of soluble products of monocyte activation, that is neopterin and interleukin 6 (IL6), by ELISA, and by quantitating the surface expression of activation markers on circulating monocytes by flow cytometry. RESULTS: Twenty-four patients with active WG were included in this study. Ten of these patients were also analysed at the time of remission. Twelve patients with sepsis served as positive controls, and 10 healthy volunteers as negative controls for monocyte activation. Patients with active disease had increased monocyte activation compared with healthy controls as shown by increased concentrations of neopterin ($p < 0.0001$) and increased surface expression of CD11b ($p < 0.05$) and **CD64** ($p < 0.05$). In those patients with increased concentrations of IL6 during active disease plasma concentrations of IL6 decreased during follow up when patients went into remission ($p < 0.0001$). In addition, neopterin ($r = 0.37$, $r = 0.44$), IL6 ($r = 0.37$, $r = 0.60$) and CD63 expression ($r = 0.39$, $r = 0.45$) correlated significantly with disease activity as measured by the Birmingham Vasculitis Activity Score and C reactive protein values, respectively. Compared with patients with sepsis, all markers of monocyte activation in patients with vasculitis were lower. CONCLUSION: It is concluded that disease activity in WG correlates with the extent of activation of monocytes, compatible with their role in the pathophysiology of this disease.

L21 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:221180 CAPLUS
DOCUMENT NUMBER: 128:281740
TITLE: Granulocytic and monocytic differentiation of CD34hi cells associated with distinct changes in the expression of the PU.1 regulated molecules, CD64 and M-CSFR
INVENTOR(S): Olweus, Johanna; Lund-Johansen, Fridtjof; Thompson, Peter
PATENT ASSIGNEE(S): Becton Dickinson and Co., USA
SOURCE: PCT Int. Appl., 46 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9814783	A1	19980409	WO 1997-US17453	19970929
W: JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6096540	A	20000801	US 1996-724725	19960930
			US 1996-724725 A	19960930

PRIORITY APPLN. INFO.:

AB The present invention demonstrates that M-CSF responsiveness and the M-CSFR expression can be used to discriminate monocytic and granulocytic cells within a population of cells which strongly expresses the CD34 antigen (CD34hi). Briefly, the method comprises isolating phenotypically and functionally defined CD34+ subsets, and staining with anti-M-CSFR monoclonal antibodies to measure expression on these primitive progenitors and cells committed to the granulocytic and monocytic lineages, based upon expression of M-CSFR. CD34hiM-CSFRhi cells are highly clonogenic and approx. 70% of the colonies are CFU-M (monocytic), whereas less than 20% were CFU-G (granulocytic). In contrast, CD34hi cells that were pos. for the granulo-monocytic marker CD64 and neg. for the M-CSFR contained high frequencies of 91% pure CFU-Gs. After 60 h in culture, CD34hiM-CSFRhi cells developed into distinct populations of M-CSFRhi and M-CSFRlo cells. These two populations gave rise almost exclusively to monocytes and granulocytes, resp. This result demonstrates that M-CSF target specificity among human hematopoietic progenitor cells is detd. by lineage-specific regulation of the M-CSFR and demonstrate that M-CSFR is a useful marker to discriminate CFU-**Ms** from CFU-Gs.

L21 ANSWER 5 OF 12 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 1999027184 MEDLINE
DOCUMENT NUMBER: 99027184 PubMed ID: 9811059
TITLE: Effects of methotrexate on differentiation of monocytes and production of cytokine inhibitors by monocytes.
AUTHOR: Seitz M; Zwicker M; Loetscher P
CORPORATE SOURCE: Department of Rheumatology, University Hospital, Inselspital, Berne, Switzerland.
SOURCE: ARTHRITIS AND RHEUMATISM, (1998 Nov) 41 (11) 2032-8. Journal code: 90M; 0370605. ISSN: 0004-3591.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981120

AB OBJECTIVE: To examine the potential of methotrexate (MTX) to act as a differentiation-stimulating factor for monocytes, which could explain the antiinflammatory properties of this agent in the treatment of rheumatoid arthritis (**RA**). METHODS: Fluorescence-activated cell sorter analysis was used to measure the changes in antigen expression (CD11b/c, CD16, **CD64**, CD14, CD68, and CD95) in response to MTX, 1,25-OH-cholecalciferol (1,25-OH-CCF), and granulocyte-**macrophage** colony-stimulating factor in the human monoblastic leukemia cell line U937, bone marrow mononuclear cells (BMMC), and peripheral blood mononuclear cells (PBMC). Release of interleukin-1beta (IL-1beta), IL-1 receptor antagonist (IL-1Ra), tumor necrosis factor a, and soluble tumor necrosis factor receptors (sTNFR) p55 and p75 during the differentiation in vitro was assessed by immunoassay in the culture supernatants. RESULTS: MTX alone and in combination with 1,25-OH-CCF markedly stimulated the differentiation of the monocytic U937 cells and simultaneously increased Fas-antigen expression. Differentiation was associated with enhanced IL-1Ra and sTNFR p75 release from U937 cells. MTX had fewer effects on phenotypic differentiation of human BMMC and PBMC, but did stimulate IL-1Ra release and inhibit IL-1beta synthesis in BMMC. CONCLUSION: MTX acts as a strong differentiation factor for immature and undifferentiated monocytic cells. Differentiation in vitro is associated with an increase in natural cytokine inhibitor release and a simultaneous down-regulation of IL-1beta. These findings may explain the marked clinical antiinflammatory effects of MTX when used in the treatment of **RA**
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L21 ANSWER 6 OF 12 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 97000804 MEDLINE
DOCUMENT NUMBER: 97000804 PubMed ID: 8843860
TITLE: The presence of interleukin-13 in rheumatoid synovium and its antiinflammatory effects on synovial fluid macrophages from patients with rheumatoid arthritis.
AUTHOR: Isomaki P; Luukkainen R; Toivanen P; Punnonen J
CORPORATE SOURCE: Turku Immunology Centre, Finland.
SOURCE: ARTHRITIS AND RHEUMATISM, (1996 Oct) 39 (10) 1693-702. Journal code: 90M; 0370605. ISSN: 0004-3591.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199611
ENTRY DATE: Entered STN: 19961219
Last Updated on STN: 19961219
Entered Medline: 19961112

AB OBJECTIVE: To study the production of interleukin-13 (IL-13) in rheumatoid synovium and the effects of recombinant IL-13 on the phenotype and function of synovial fluid (SF) **macrophages** and T cells derived from patients with rheumatoid arthritis (**RA**). METHODS: The presence of IL-13 in SF was studied using an IL-13-specific enzyme-linked immunosorbent assay (ELISA); the production of IL-13 was studied in SF mononuclear cells (SFMC) by reverse transcriptase-polymerase chain reaction. The effects of recombinant IL-13 on cytokine production by and phenotype of SFMC were evaluated using cytokine-specific ELISAs and flow cytometry, respectively. The effect of IL-13 on the proliferation of SFMC was determined by 3H-thymidine incorporation. The production and the effects of IL-13 were compared with those of IL-4. RESULTS: IL-13 was present in 27 of 28 SF samples, and IL-13 messenger RNA (mRNA) was detectable in SFMC. Importantly, IL-13 levels were significantly higher than those of IL-4, and IL-13 protein and mRNA were expressed in several samples, although IL-4 synthesis was undetectable. Recombinant IL-13 significantly reduced the production of IL-1 beta and tumor necrosis factor alpha and the expression of CD16 and **CD64** by SF **macrophages**, whereas the expression of HLA-DR and CD23 was

increased. These effects on SF **macrophages** were similar to those observed with IL-4, but in contrast to IL-4, IL-13 had no growth-promoting effect on SF T cells. CONCLUSION: IL-13 is consistently present in rheumatoid synovium. The ability of exogenous IL-13 to decrease the production of proinflammatory cytokines by SFMC suggests that it may have therapeutic potential in the treatment of patients with **RA**.

L21 ANSWER 7 OF 12 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 96193599 MEDLINE
DOCUMENT NUMBER: 96193599 PubMed ID: 8607887
TITLE: Interleukin-10 functions as an antiinflammatory cytokine in rheumatoid synovium.
AUTHOR: Isomaki P; Luukkainen R; Saario R; Toivanen P; Punnonen J
CORPORATE SOURCE: Turku University, Finland.
SOURCE: ARTHRITIS AND RHEUMATISM, (1996 Mar) 39 (3) 386-95.
Journal code: 90M; 0370605. ISSN: 0004-3591.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199605
ENTRY DATE: Entered STN: 19960531
Last Updated on STN: 19960627
Entered Medline: 19960521

AB OBJECTIVE: Interleukin-10 (IL-10) is an antiinflammatory cytokine that has been shown to play a role in rheumatoid arthritis (**RA**). We therefore investigated the effects of IL-10 on the function and phenotype of synovial fluid mononuclear cells (SFMC) derived from patients with **RA**. In addition, we studied the production of IL-10 in rheumatoid joints, and the role of endogenous IL-10 in the regulation of SFMC function. METHODS: The presence of IL-10 in rheumatoid joints was studied using IL-10-specific enzyme-linked immunosorbent assay (ELISA) and reverse transcriptase- polymerase chain reaction (RT-PCR) techniques. The effects of recombinant human IL-10 or neutralizing anti-IL-10 monoclonal antibodies (MAbs) on both cytokine production and phenotype of SFMC were evaluated using cytokine-specific ELISAs and flow cytometry. The effect of IL-10 on proliferation of SFMC was determined by incorporation of tritiated thymidine. RESULTS: IL-10 was detected by ELISA in 22 of 23 SF samples, and was spontaneously produced by cultured SFMC. IL-10 messenger RNA was detectable in all 8 SFMC samples, as determined by RT-PCR. Neutralization of endogenously produced IL-10 by anti- IL-10 MAbs resulted in increased production of IL-1 beta, tumor necrosis factor alpha (TNF alpha), and granulocyte- **macrophage** colony-stimulating factor (GM-CSF) by SFMC, and in enhanced proliferation of SFMC. In particular, the production of TNFalpha was dramatically increased by anti-IL-10 MAbs. Moreover, the expression of HLA-DR molecules by SF **macrophages** was increased, and the expression of CD16 was decreased by anti-IL-10 MAbs. In contrast, addition of recombinant IL-10 significantly decreased the production of IL-1 beta, TNF alpha, and GM-CSF by SFMC, and decreased spontaneous and IL-2-induced proliferation of SFMC. Finally, IL-10 decreased HLA-DR expression and increased the expression of the Fc gamma receptors, CD16 and **CD64**, by SF **macrophages**. CONCLUSION: These data indicate that endogenously produced IL-10 functions as an immunoregulatory molecule in rheumatoid synovium. Importantly, exogenous IL-10 has potent antiinflammatory effects on SFMC, suggesting that IL-10 may be useful in the treatment of patients with **RA**.

L21 ANSWER 8 OF 12 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 96128145 MEDLINE
DOCUMENT NUMBER: 96128145 PubMed ID: 8536370
TITLE: Changes in the phenotype of monocytes/macrophages and expression of cytokine mRNA in peripheral blood and synovial fluid of patients with rheumatoid arthritis.
AUTHOR: Highton J; Carlisle B; Palmer D G
CORPORATE SOURCE: Department of Medicine, University of Otago Medical School, Dunedin, New Zealand.
SOURCE: CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (1995 Dec) 102 (3) 541-6.
Journal code: DD7; 0057202. ISSN: 0009-9104.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199602
ENTRY DATE: Entered STN: 19960221
Last Updated on STN: 19960221
Entered Medline: 19960208

AB Data from a previous study suggested that peripheral blood monocytes in patients with rheumatoid arthritis (**RA**) may be activated. Therefore, in this study we sought further evidence of 'presynovial' activation of monocytes. Our results show that phenotypic changes are demonstrable in peripheral blood monocytes in patients with **RA**, including increased expression of CR3 (CD11b/CD18) and FcRI (**CD64**). However, changes are most extensive in synovial monocytes/**macrophages** and especially for HLA-DR and intercellular adhesion molecule-1 (ICAM-1) (CD54). We conclude that monocyte/**macrophage** activation is most evident within the joint, and that 'presynovial' changes occur but are of limited extent.

L21 ANSWER 9 OF 12 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 94209976 MEDLINE
DOCUMENT NUMBER: 94209976 PubMed ID: 8158203
TITLE: Reactive microglia in multiple sclerosis lesions have an increased expression of receptors for the Fc part of IgG.
AUTHOR: Ulvestad E; Williams K; Vedeler C; Antel J; Nyland H; Mork S; Matre R
CORPORATE SOURCE: Department of Microbiology and Immunology, Gade Institute, University of Bergen, Norway.
SOURCE: JOURNAL OF THE NEUROLOGICAL SCIENCES, (1994 Feb) 121 (2) 125-31.
Journal code: JBJ; 0375403. ISSN: 0022-510X.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199405
ENTRY DATE: Entered STN: 19940526
Last Updated on STN: 19940526
Entered Medline: 19940516

AB Receptors for the Fc part of IgG, FcRI (**CD64**), FcRII (CD32), and FcRIII (CD16) were studied by indirect immunoperoxidase staining of cryostat sections from normal and multiple sclerosis (**MS**) brains. Microglia in the parenchyma of normal white matter had a dendritic

morphology, and were weakly stained by monoclonal antibodies (mAbs) to FcRI, FcRII, and FcRIII. In active **MS** lesions reactive microglia were strongly stained by the mAbs 32.2 (FcRI), IV-3 (FcRII), and 3G8 (FcRIII). Perivascular **macrophages** were stained by all anti-FcR mAbs in both normal white matter and in **MS** lesions, whereas endothelial cells were stained by the anti-FcRIII mAb only. The FcR on microglia and perivascular **macrophages** may be of functional importance in antibody-dependent cell-mediated cytotoxicity (ADCC), phagocytosis, and local immunoregulation. FcR on endothelium may be of importance in binding and transportation of immune complexes into the CNS. FcR mediated functions may consequently be highly relevant to the pathogenesis of **MS**.

L21 ANSWER 10 OF 12 MEDLINE
ACCESSION NUMBER: 94065191 MEDLINE
DOCUMENT NUMBER: 94065191 PubMed ID: 7902377
TITLE: Effects of IL-13 on phenotype, cytokine production, and cytotoxic function of human monocytes. Comparison with IL-4 and modulation by IFN-gamma or IL-10.
AUTHOR: de Waal Malefyt R; Figdor C G; Huijbens R; Mohan-Peterson S; Bennett B; Culpepper J; Dang W; Zurawski G; de Vries J E
CORPORATE SOURCE: Department of Human Immunology, DNAX Research Institute of Molecular and Cellular Biology, Palo Alto, CA 94304-1104.
SOURCE: JOURNAL OF IMMUNOLOGY, (1993 Dec 1) 151 (11) 6370-81. Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199401
ENTRY DATE: Entered STN: 19940201
Last Updated on STN: 19950206
Entered Medline: 19940106

AB Recently, we described the cloning and expression of a human cDNA which is the homologue to P600, a gene transcribed by mouse Th2 clones. Based on its activities on human monocytes and B cells this gene was designated IL-13. In the present study we investigated the effects of IL-13 alone or in combination with IL-4, IFN-gamma, or IL-10 on human monocytes. IL-13 induced significant changes in the phenotype of monocytes. Like IL-4, it enhanced the expression of CD11b, CD11c, CD18, CD29, CD49e (VLA-5), class II MHC, CD13, and CD23, whereas it decreased the expression of **CD64**, CD32, CD16, and CD14 in a dose-dependent manner. IL-13 induced up-regulation of class II MHC Ag and its down-regulatory effects on **CD64**, CD32, and CD16 expression were prevented by IL-10. IFN-gamma could also partially prevent the IL-13-induced down-regulation of **CD64**, but not that of CD32 and CD16. However, IL-13 strongly inhibited spontaneous and IL-10- or IFN-gamma-induced ADCC activity of human monocytes toward anti-D coated Rh+ erythrocytes, indicating that the cytotoxic activity of monocytes was inhibited. Furthermore, IL-13 inhibited production of IL-1 alpha, IL-1 beta, IL-6, IL-8, IL-10, IL-12 p35, IL-12 p40, **macrophage** inflammatory protein-1 alpha, granulocyte/**macrophage**-CSF, granulocyte-CSF, IFN-alpha, and TNF alpha by monocytes activated with LPS. In contrast, IL-13 enhanced the production of IL-1 **ra** by these cells. Similar results on cytokine production were observed or have been obtained with IL-4. Thus IL-13 shares most of its activities on human monocytes with IL-4, but no additive or synergistic effects of IL-4 and IL-13 on human monocytes were observed, suggesting that these cytokines may share common receptor components. Taken together, these results indicate that IL-13 has anti-inflammatory and important immunoregulatory activities.

L21 ANSWER 11 OF 12 MEDLINE
ACCESSION NUMBER: 94282010 MEDLINE
DOCUMENT NUMBER: 94282010 PubMed ID: 8012331
TITLE: [Macrophages in rheumatoid synovial membrane: an update]. Les macrophages de la synoviale rhumatoide: une mise au point.
AUTHOR: Demaziere A
CORPORATE SOURCE: Universite d'Oxford, Service d'Anatomie Pathologique, Centre Orthopedique Nuffield.
SOURCE: REVUE DU RHUMATISME. EDITION FRANCAISE, (1993 Oct) 60 (9) 568-79. Ref: 56
Journal code: BQU; 9315664.
PUB. COUNTRY: France
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199407
ENTRY DATE: Entered STN: 19940810
Last Updated on STN: 19940810
Entered Medline: 19940727

AB The immunophenotype of lining and subintimal synovial mononuclear phagocytes (MP) of rheumatoid arthritis (**RA**) were sought by immunohistology and compared with osteoarthritis (OA) tissue in order to determine the significance of MPs in the pathobiology of **RA**. Almost all the lining cells (SLCs) in **RA** consisted of MPs (80 to 90% expressing CD45/CD14/CD68). A major proportion of the interaggregate areas of the rheumatoid subintima was also made of MP cells (50 to 70% expressing CD14/CD68). A marked variation in the immunohistological reaction of antibodies reacting within intimal MPs and between intimal and subintimal MPs was found. Intimal MPs expressed a wide range of **macrophage**-associated antigens, including receptors for Fc (CD16, CD32, **CD64**) and complement (CD35, CD11b, CD11c) as well as several integrin and non-integrin cell adhesion molecules (CD29/CD49b, CD49d, CD49f, CD51/CD61, CD11a, CD31, CD54, CD44, CD9, CD63). The monocyte marker, CD14, was down-regulated on SLCs in both **RA** and OA. When compared to intimal expression of leucocyte common antigen (CD45), CD68, a pan-**macrophage** maturation antigen, was found to be an unreliable **macrophage** antigen in OA intima. There was no difference in antigenic phenotype of SLCs in inflammatory and non-inflammatory OA with early activation markers (CD25, CD71) mainly present on MPs. In **RA** , synovial MPs showed increased expression of activation, maturation and functional antigens suggesting that they are rapidly and fully activated. The fact that their recruitment was independent of the degree of lymphocyte infiltration further emphasises the central importance of synovial MPs in **RA**.

L21 ANSWER 12 OF 12 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 93337028 EMBASE
DOCUMENT NUMBER: 1993337028
TITLE: Macrophages in arthritic synovium: A general reappraisal.

AUTHOR: Demaziere A.
CORPORATE SOURCE: France
SOURCE: Revue du Rhumatisme (English Edition), (1993) 60/9 (473-483).
ISSN: 1169-8446 CODEN: RRHUEX
COUNTRY: France
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 020 Gerontology and Geriatrics
026 Immunology, Serology and Transplantation
031 Arthritis and Rheumatism
LANGUAGE: English
SUMMARY LANGUAGE: English; French; German

AB The immunophenotype of lining and subintimal synovial mononuclear phagocytes (MP) of rheumatoid arthritis (**RA**) were sought by immunohistology and compared with osteoarthritis (OA) tissue in order to determine the significance of MPs in the pathobiology of **RA**. Almost all the lining cells (SLCs) in **RA** consisted of MPs (80 to 90% expressing CD45/CD14/CD68). A major proportion of the interaggregate areas of the rheumatoid subintima was also made of MP cells (50 to 70% expressing CD14/CD68). A marked variation in the immunohistological reaction of antibodies reacting within intimal MPs and between intimal and subintimal MPs was found. Intimal MPs expressed a wide range of **macrophage**-associated antigens, including receptors for Fc (CD16, CD32, **CD64**) and complement (CD35, CD11b, CD11c) as well as several integrin and non-integrin cell adhesion molecules (CD29/CD49h, CD49d, CD49f, CD51/CD61, CD11a, CD31, CD54, CD44, CD9, CD63). The monocyte marker, CD14, was down-regulated on SECs in both **RA** and OA. When compared to intimal expression of leucocyte common antigen (CD45), CD68, a pan-**macrophage** maturation antigen, was found to be an unreliable **macrophage** antigen in OA intima. There was no difference in antigenic phenotype of SLCs in inflammatory and non-inflammatory OA with early activation markers (CD25, CD71) mainly present on MPs. In **RA**, synovial MPs showed increased expression of activation, maturation and functional antigens suggesting that they are rapidly and fully activated. The fact that their recruitment was independent of the degree of lymphocyte infiltration further emphasises the central importance of synovial MPs in **RA**.

=> dis his

(FILE 'HOME' ENTERED AT 09:36:34 ON 05 APR 2002)

FILE 'MEDLINE, CAPLUS, EMBASE' ENTERED AT 09:36:54 ON 05 APR 2002

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L1            7 S FCGAMMAR1
L2           65 S FC (1N) GAMMA (1N) R1
L3         1957 S FC (1N) GAMMA (1N) RI
L4          982 S CD64
L5            0 S L1 AND L2 AND L3 AND L4
L6         2547 S L1 OR L2 OR L3 OR L4
L7         1130 S L6 (P) ANTIBOD?
L8           54 S L7 (P) ADMINIST?
L9           26 DUP REM L8 (28 DUPLICATES REMOVED)
L10         585 S VAN DE WINKEL?/AU
L11        1074 S L10 AND MACROPHAGE? OR CD64
L12         183 S L10 AND (MACROPHAGE? OR CD64)
L13         127 S L12 (P) ANTIBOD?
L14          11 S L13 (P) ADMINIST?
L15           7 DUP REM L14 (4 DUPLICATES REMOVED)
L16         299 S L4 (P) MACROPHAGE?
L17           0 S L16 AND PSORIASIS
L18          10 S L16 AND (HIV)
L19           5 DUP REM L18 (5 DUPLICATES REMOVED)
L20          23 S L16 AND (LUPUS OR SCLERODERMA OR DERMATITIS OR WEGENER? OR RA
L21          12 DUP REM L20 (11 DUPLICATES REMOVED)

=> s (mab (1N) 22) or H22 or (CRL (1N) 1117)
L22         816 (MAB (1N) 22) OR H22 OR (CRL (1N) 1117)

=> s l22 (p) administ?
L23          58 L22 (P) ADMINIST?

=> dup rem l23
PROCESSING COMPLETED FOR L23
L24          35 DUP REM L23 (23 DUPLICATES REMOVED)

=> s l24 and not l7
MISSING TERM 'AND NOT'
The search profile that was entered contains a logical
operator followed immediately by another operator.

=> s l24  not l7
L25          33 L24 NOT L7

=> dis l25 1-33 ibib abs

L25  ANSWER 1 OF 33     MEDLINE
ACCESSION NUMBER:   2002071306     MEDLINE
DOCUMENT NUMBER:    21656446   PubMed ID: 11797219
TITLE:              Expression and purification of murine interleukin 18 in
                    Escherichia coli and its antitumor effects.
AUTHOR:             Zhou H; Zhao H R; Pei D S; Lu L; Hu S Q
CORPORATE SOURCE:   Research Center for Biochemistry and Molecular Biology,
                    Xuzhou Medical College, Xuzhou 221002, China.
SOURCE:             SHENG WU KUNG CH ENG HSUEH PAO, (2001 Sep) 17 (5) 548-52.
                    Journal code: 9426463. ISSN: 1000-3061.
PUB. COUNTRY:       China
                    Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           Chinese
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200202
ENTRY DATE:         Entered STN: 20020125
                    Last Updated on STN: 20020227
                    Entered Medline: 20020226
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AB Total RNA was extracted from murine hepatocytes, and the cDNA of interleukin 18(IL-18) was amplified by RT-PCR. The cDNA was introduced into the expression vector pJW2 and sequenced. Under heat induction, the recombinant murine IL-18(rmIL-18) was expressed in inclusion bodies in E. coli with the yield accounting for 18% of total bacteria proteins. The inclusion bodies were dissolved with 5 mol/L urea, and rmIL-18 was purified using Sephadex G-100 column chromatography. In the presence of 0.5 mg/L Con A, the purified rmIL-18 showed dose-dependent IFN-gamma-inducing activity in murine splenocytes. The purified rmIL-18

exhibited significant antitumor effects in Kunming mice challenged intraperitoneally (i.p.) with **H22** hepatocarcinoma when **administered** 10 micrograms rmIL-18 i.p. on days 1, 4 after challenge, and the mice survived resisted the rechallenged with **H22** cells.

L25 ANSWER 2 OF 33 MEDLINE
ACCESSION NUMBER: 2001549852 MEDLINE
DOCUMENT NUMBER: 21480802 PubMed ID: 11596291
TITLE: Use of monoclonal antibody-pinyangmycin conjugate in experimental regional targeting therapy of tumor.
AUTHOR: Wang W G; Xu L N; Zhang S H; Xue Y C; Zhen Y S
CORPORATE SOURCE: Institude of Medicinal Biotechnology, Chinese Academy of Medical Science and Peking Union Medical College, Beijing 100050.
SOURCE: YAO HSUEH HSUEH PAO [ACTA PHARMACEUTICA SINICA], (1997 Sep) 32 (9) 669-74.
Journal code: 21710340R. ISSN: 0513-4870.
PUB. COUNTRY: China
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011015
Last Updated on STN: 20020124
Entered Medline: 20011231

AB McAb 3A5, a rat monoclonal antibody, was linked to pingyangmycin (PYM), an antitumor antibiotic identical to bleomycin A5 currently in clinical use, employing Dextran T-40 as an intermediate agent. The 3A5-PYM conjugate retained complete immunoreactivity of McAb 3A5. Determined by clonogenic assay with colon cancer HT-29 cells, the IC50 values for 3A5-PYM conjugate and free PYM were 0.6 mumol.L-1 and 10.2 mumol.L-1, respectively. Hepatoma **H22** ascites was transplanted into the peritoneal or thoracic cavity of mice. On the next day, 3A5-PYM or PYM, were injected into the cavity. Therapeutic effect was evaluated on the survival time of mice. For intraperitoneal tumor, the ILS(%) values were 238% for 3A5-PYM and 40% for PYM. For intrapleural tumor, the ILS(%) values were 384% for 3A5-PYM and 66% for PYM. Murine hepatoma **H22** was transplanted s.c. into mice and 3A5-PYM conjugate or free PYM were injected peritumorally. As determined by antimicrobial assay, the **administration** of 3A5-PYM showed higher concentration and longer retention time in the tumor than that of free PYM. Tumor fragments of human colon cancer HT-29 were transplanted s.c. into nude mice. Then 3A5-PYM or PYM was injected i.v., i.p. or pt (peritumorally) 3 days after inoculation, twice a week, with a total of 7 injections. Tumor growth inhibition was evaluated 4 weeks later. The inhibition rates on the growth of colon cancer xenografts were as follows: (1) for i.v. route, 58% by PYM, 79% by 3A5-PYM; (2) for i.p. route, 52% by PYM, 61% by 3A5-PYM; and (3) for pt route, 73% by PYM, 96% by 3A5-PYM. These results indicate that 3A5-PYM conjugate is highly effective against targeted human cancer xenograft and mouse tumor when **administered** peritumorlly or intracavitarily.

L25 ANSWER 3 OF 33 MEDLINE
ACCESSION NUMBER: 2001273799 MEDLINE
DOCUMENT NUMBER: 21259190 PubMed ID: 11360680
TITLE: Effects of glutamine on tumor growth and apoptosis of hepatoma cells.
AUTHOR: Liu S L; Shi D Y; Shen Z H; Wu Y D
CORPORATE SOURCE: Department of Biochemistry, Shanghai Medical University, Shanghai 200032, China.. slliu@shmu.edu.cn
SOURCE: Acta Pharmacol Sin, (2000 Jul) 21 (7) 668-72.
Journal code: DPS; 100956087.
PUB. COUNTRY: China
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010702
Last Updated on STN: 20010702
Entered Medline: 20010628

AB AIM: To explore the effects of glutamine on growth and apoptosis of hepatoma cells. METHODS: Mice inoculated with hepatoma cell (**H22**) suspension subcutaneously at right axilla were orally **administered** with glutamine (GLN) solution. Human hepatoma cell culture (SMMC-7721) was treated with different concentrations of GLN solution. The content of malondialdehyde (MDA) and nitric oxide (NO) was detected in mice plasma and cell culture, and that of glutathione (GSH) was decected in cells. The inoculated tumor's growth in the mice and hepatoma cells' proliferation and apoptosis were observed. RESULTS: When mice were **administered** orally with GLN solution (300 mg/kg), the growth of inoculated hepatoma was suppressed in the mice. When different concentrations of GLN solution were added in human hepatoma cell culture, the hepatoma cells' proliferation was inhibited and cells were induced to apoptosis, which was dependent on GLN concentration; meanwhile the contents of NO rose both in mice plasma and in cell culture, however MDA contents were slightly lowered in both, and the activity of GSH increased in the cells which had been ultrasonically shattered. CONCLUSION: Hepatoma cell apoptosis and tumor growth inhibition by GLN may be associated with its antioxidative activity and its intervention in hepatoma cell proliferation, and simultaneous release of NO.

L25 ANSWER 4 OF 33 MEDLINE
ACCESSION NUMBER: 2001160620 MEDLINE
DOCUMENT NUMBER: 21158756 PubMed ID: 11261201
TITLE: Anticancer effect of Howiinol A and its mechanism of action.
AUTHOR: Xu C X; He J H
CORPORATE SOURCE: Department of Pharmacology I, Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, 1 Xian Nong Tan Street, Beijing 100050, China.. xcx@mdsharris.com@INET
SOURCE: J Asian Nat Prod Res, (1999) 2 (1) 1-19.
Journal code: D07; 100888334. ISSN: 1028-6020.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010604
Last Updated on STN: 20010604
Entered Medline: 20010531

AB Howiinol A (GHM-10) is a kind of phenylethylene pyrone compounds isolated from Goniothalamus howii. By using the techniques of cell growth curve

determination, MTT test, soft agar colony assay and experimental therapy of transplantable tumors in mice, it is found that GHM-10 exerts potent inhibitory effect on cancer cells but its influence on normal cells is relatively slight; the sensitivity of a drug-resistant cell line, KB/VCR 2000, to GHM-10 is similar to its parent cell line KB. Remarkable therapeutic effect can be seen in mice bearing **H22** hepatoma and Lewis lung cancer and in mice with ascetic sarcoma 180 when GHM-10 is orally or intraperitoneally **administered**. The IC50s of L1210 cells treated with GHM-10 for 1 and 24 h are 6.85 and 3.32 micrograms.ml-1 respectively. The ratio of IC50 1 h and IC50 24 h is only 2.06, indicating that the action of GHM-10 is conformed to a cell cycle non-specific cytotoxic agent. By using trypan blue exclusive test and morphological examination, it is demonstrated that the main effect of GHM-10 is to inhibit the cell proliferation. Flow cytometery technique is used to analyze the cell cycle of L1210 cells. The results show that to some extent, GHM-10 blocks the cell cycle transition from G1 phase to S phase. By using [3H] labeled precursor incorporation technique, it is shown that GHM-10 significantly suppresses the biosynthesis of DNA, RNA and protein in L1210 cells, and the DNA synthesis is mostly affected. At 1 h after the cells were treated with GHM-10, these inhibitory effects have already been irreversible, suggesting that GHM-10 may cause structural damage on DNA molecules. However, GHM-10 is unable to intercalate into DNA molecules or to destroy its structure directly. By using single cell gel electrophoresis and alkaline elution technology, it is confirmed that GHM-10 causes DNA molecule damage and single strand breakage in L1210 cells. Further studies show that GHM-10 markedly inhibits DNA dehelix induced by DNA topoisomerase II both inside and outside the cells, indicating that GHM-10 is acting as an inhibitor of DNA topoisomerase II.

L25 ANSWER 5 OF 33 MEDLINE
ACCESSION NUMBER: 2001119678 MEDLINE
DOCUMENT NUMBER: 21073845 PubMed ID: 11205875
TITLE: Roles of Se and NO in apoptosis of hepatoma cells.
AUTHOR: Liu S; Shia D; Liu G; Chen H; Liu S; Hu Y
CORPORATE SOURCE: Department of Biochemistry, Medical college of Fudan University, Shanghai, People's Republic of China.. slliu@shmu.edu.cn
SOURCE: LIFE SCIENCES, (2000 Dec 29) 68 (6) 603-10.
Journal code: L62. ISSN: 0024-3205.
PUB. COUNTRY: England: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010215

AB Mice inoculated with hepatoma cell (**H22**) suspension subcutaneously at their right axilla were **administered** orally with kappa-selenocarrageenan (Se) solution, the inoculated hepatoma's growth was suppressed. Different concentrations of Se solution added in human hepatoma cell line culture could inhibit proliferation and induce apoptosis in hepatoma cells. Meanwhile Se solution could increase the activity of glutathione peroxidase (GSH-Px) in the mice's plasma and the content of NO in the mice's sera and the hepatoma cell culture supernatant as well. Therefore, apoptosis in hepatoma cell induced by Se solution may be associated with the increase in antioxidative activity, the suppression free radical's intervention, and the excessive release of NO by stress.

L25 ANSWER 6 OF 33 MEDLINE
ACCESSION NUMBER: 2000147190 MEDLINE
DOCUMENT NUMBER: 20147190 PubMed ID: 10682609
TITLE: Study on inhibition and prevention of tumor and antioxidative effects of lithium carbonate in tumor bearing mice.
AUTHOR: Zhang A; Huang X; Luo P; Jiang X
CORPORATE SOURCE: Department of Public Health, Guiyang Medical College, China.
SOURCE: WEI SHENG YEN CHIU [JOURNAL OF HYGIENE RESEARCH], (1998 Mar) 27 (2) 77-80.
Journal code: CPB; 9426367. ISSN: 1000-8020.
PUB. COUNTRY: China
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000407
Last Updated on STN: 20000407
Entered Medline: 20000324

AB Two Kinds of tumor-bearing mice (hepatoma **H22** and sarcoma S180) were **administered** with lithium carbonate (Li2CO3) for 17 or 10 days (advanced and simultaneous **administration**), in order to observe the effects of prevention and treatment of Li2CO3 on malignant tumor, as well as the relationship between Li2CO3 and lipid peroxidation in tumor-bearing mice. Meanwhile, we compared the toxic and side effects of cyclophosphamide (CP) with that of Li2CO3. The results showed that Li2CO3 had no significant toxic or side effects with the suggested doses. In the tests of inhibition and prevention of tumor, Li2CO3 could significantly inhibit the grouth of the two kinds of tumor, and increase the activity of superoxide dismutage (SOD) and decrease the contents of Malonyldialdehyde (MDA). In addition, Li2CO3 had no effect on the white blood cells (WBC) and decreased the micronucleus frequency (MNF) in bone marrow polychromatic erythrocytes (PCE), while CP had definite effect of decreasing the WBC and increasing the MNF in the tumor-bearing mice.

L25 ANSWER 7 OF 33 MEDLINE
ACCESSION NUMBER: 97440609 MEDLINE
DOCUMENT NUMBER: 97440609 PubMed ID: 9294827
TITLE: The role of complement in the pathogenesis of tubulointerstitial lesions in rat mesangial proliferative glomerulonephritis.
AUTHOR: Morita Y; Nomura A; Yuzawa Y; Nishikawa K; Hotta N; Shimizu F; Matsuo S
CORPORATE SOURCE: Third Department of Internal Medicine, Nagoya University School of Medicine, Japan.
SOURCE: JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY, (1997 Sep) 8 (9) 1363-72.
Journal code: A6H; 9013836. ISSN: 1046-6673.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199710

ENTRY DATE: Entered STN: 19971224
Last Updated on STN: 19971224
Entered Medline: 19971028

AB Persistent proteinuria and tubulointerstitial lesions are important signs of progressive renal disease. The purpose of this study was to assess the role of complement in the development of tubulointerstitial lesions in rats with proteinuria due to primary glomerulonephritis. Mesangial proliferative glomerulonephritis was induced in mononephrectomized rats by intravenous injection of monoclonal antibody (**mAb**) 1-**22**-3 (Clin Exp Immunol 102: 181-185, 1995). As early as 24 h after the injection, proteinuria became evident, persisted throughout the observation period, and was associated with mesangial cell proliferation and tubulointerstitial lesions when examined at 7 and 14 d after mAb **administration**. Deposition of rat C3 and C5b-9 was observed at the luminal surface of proximal tubules and in cellular debris present in the tubular lumen (group I). Rats injected with **mAb** 1-**22**-3 and depleted of complement by injections of cobra venom factor starting at day 3 developed glomerulonephritis and proteinuria comparable to rats of group I, but complement deposition in the tubules and the tubulointerstitial lesions were markedly reduced (group II). Rats in group III were injected with mAb and, from day 3, with soluble complement receptor type 1, which became detectable at the luminal surface of proximal tubules and in the urine. Deposition of C5b-9 in tubular cells was not detectable, and the severity of tubulointerstitial lesions was reduced compared with rats in group I. These results indicate that, in this model of primary mesangial proliferative glomerulonephritis with proteinuria, the development of tubulointerstitial lesions is associated with activation of serum complement at the level of tubular brush border, and tubulointerstitial lesions can be reduced by inhibition of complement activity.

L25 ANSWER 8 OF 33 MEDLINE
ACCESSION NUMBER: 95066899 MEDLINE
DOCUMENT NUMBER: 95066899 PubMed ID: 7976390
TITLE: Antitumor activity of thevetoside alone and in combination with chlormethine in vivo.
AUTHOR: Zhang X W; Huang Z Q; Li C C
CORPORATE SOURCE: Department of Pharmacology, Fujian Medical College, Fuzhou, China.
SOURCE: CHUNG-KUO YAO LI HSUEH PAO [ACTA PHARMACOLOGICA SINICA], (1994 May) 15 (3) 285-8.
Journal code: 1P9; 8100330. ISSN: 0253-9756.
PUB. COUNTRY: China
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199412
ENTRY DATE: Entered STN: 19950110
Last Updated on STN: 19950110
Entered Medline: 19941208

AB Thevetoside (TS) is one of the cardiac glycosides. A study of antitumor activity was carried out in 6 types of murine tumors in vivo, such as the ascitic tumors **H22**, EAC, P388, and solid tumors S180, U14, Lewis lung carcinoma, which were treated with i.p. TS 1.5 mg.kg-1.d-1 alone or in combination with chlormethine (Chl) 0.3, 0.5, or 1.0 mg.kg-1.d-1. TS only showed a remarkable inhibition on the growth of 3 types of solid tumors with inhibition rates of 48.7%-56.7%. The effect of the combination therapy was much pronounced than that of independent **administration**. The life span under combined therapy was increased 82.4% to > 122.1%. For solid tumors, the combined **administration** gave inhibition rates of 65.6%-72.5%.

L25 ANSWER 9 OF 33 MEDLINE
ACCESSION NUMBER: 94085173 MEDLINE
DOCUMENT NUMBER: 94085173 PubMed ID: 8261861
TITLE: In-vitro and in-vivo studies on the antitumor activity of LICC in Km mice.
AUTHOR: Li X M
CORPORATE SOURCE: Nanjing Railway Medical College.
SOURCE: CHUNG-HUA CHUNG LIU TSA CHIH [CHINESE JOURNAL OF ONCOLOGY], (1993 May) 15 (3) 185-8.
Journal code: EBH; 7910681. ISSN: 0253-3766.
PUB. COUNTRY: China
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199401
ENTRY DATE: Entered STN: 19940209
Last Updated on STN: 19970203
Entered Medline: 19940124

AB In order to investigate a more efficient effector cell than the classical LAK cell in tumor immunotherapy, anti-tumor activity of lymphokine-induced cytotoxic cell (LICC) was studied. The results showed that LICC had greater cytotoxicity to YAC-1, HL60, P815 and **H22** tumor cells in vitro than the control spleen cells. In vivo, LICC revealed a prominent inhibiting effect on the growth of **H22** cells. A mixture of LICC and **H22** in the ratio of 100: 1 was injected subcutaneously into the subaxillary tissue of Km mice (Group 1). Tumor developed in 8% of the experimental animals within 10 weeks, while all of the control animals inoculated with **H22** cells died from tumor in the same period ($P < 0.001$). In the other groups, **H22** cells were injected as in group 1, but the LICC cells were **administered** through the tail vein (Group 2) or to the abdominal cavity (Group 3) once every week. In group 2, tumor developed in 25% of the experimental mice and 100% of the control mice ($P < 0.001$). In group 3, there was no significant difference in the frequency of tumor development between the experimental and control animals.

L25 ANSWER 10 OF 33 MEDLINE
ACCESSION NUMBER: 93251708 MEDLINE
DOCUMENT NUMBER: 93251708 PubMed ID: 8485917
TITLE: Increased limb involvement in murine collagen-induced arthritis following treatment with anti-interferon-gamma.
AUTHOR: Williams R O; Williams D G; Feldmann M; Maini R N
CORPORATE SOURCE: Kennedy Institute of Rheumatology, incorporating Charing Cross Sunley Research Centre, London, UK.
SOURCE: CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (1993 May) 92 (2) 323-7.
Journal code: DD7; 0057202. ISSN: 0009-9104.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199306
ENTRY DATE: Entered STN: 19930618
Last Updated on STN: 19930618
Entered Medline: 19930608

AB We have tested the effect of **administering H22**, a hamster neutralizing MoAb to murine interferon-gamma (IFN-gamma) in collagen-induced arthritis. Mice were immunized with human type II collagen in adjuvant on day 1 and boosted with soluble collagen on day 21. **H22** was **administered** (250 micrograms, intraperitoneally) either during the induction of arthritis (on days 0, 6, 13 and 20) or around the time of disease manifestation (on days 21, 28, 35 and 42). Control mice received either an isotype-matched non-neutralizing MoAb or saline. Both treatment regimes gave similar results. Treatment with **H22** did not significantly affect the incidence of arthritis, time of onset, degree of oedema, histopathological severity, or level of anti-type II collagen IgG. However, a highly significant increase ($P < 0.01$) in the number of limbs affected by arthritis was observed in the **H22**-treated group, irrespective of whether the antibody was **administered** during the induction of arthritis, or during the time of clinical manifestation of disease. From these results it was concluded that anti-IFN-gamma treatment caused an increase in the number of arthritic lesions, but did not affect the severity of each individual lesion.

L25 ANSWER 11 OF 33 MEDLINE
ACCESSION NUMBER: 90257415 MEDLINE
DOCUMENT NUMBER: 90257415 PubMed ID: 2111356
TITLE: Protective activity of recombinant murine tumor necrosis factor-alpha and interferon-gamma against experimental murine lung carcinoma metastases.
AUTHOR: Schultz R M; Altom M G
CORPORATE SOURCE: Department of Immunology Research, Lilly Research Laboratories, Indianapolis, IN 46285.
SOURCE: JOURNAL OF INTERFERON RESEARCH, (1990 Apr) 10 (2) 229-36.
Journal code: IJI; 8100396. ISSN: 0197-8357.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199006
ENTRY DATE: Entered STN: 19900720
Last Updated on STN: 19900720
Entered Medline: 19900625

AB A variety of biologic and synthetic agents protect BALB/c mice against experimental M109 micrometastases. We have presented evidence that eradication of these metastases is mediated by the activation of host macrophages to the tumoricidal state. We now present evidence that injection of **H22**, a neutralizing hamster IgG monoclonal antibody to murine interferon-gamma (IFN-gamma; macrophage activating factor), 2 days prior to i.v. tumor inoculation markedly increases the metastatic capacity of M109 lung carcinoma cells. Therefore, we tested several cytokines that induce or mediate macrophage-mediated cytotoxicity, including IFN-gamma, tumor necrosis factor-alpha, and interleukin-1 beta (IL-1 beta), for their ability to inhibit the development of experimental M109 lung metastases. Intraperitoneal treatment with recombinant murine (rMu) IFN-gamma (greater than or equal to 10,000 units/mouse) or recombinant murine TNF-alpha (greater than or equal to 10,000 units/mouse) produced greater than 60% inhibition of metastasis formation. Optimal therapy was observed when cytokines were **administered** 2 days prior to i.v. tumor cell inoculation. Neither IFN-gamma nor TNF-alpha inhibited colony formation of M109 cells in vitro, suggesting a host-mediated mechanism for antitumor activity. Peritoneal macrophages were primed for tumor cytotoxicity by treatment with either IFN-gamma or TNF-alpha. Intraperitoneal treatment with recombinant human IL-1 beta (1 X 10(5) units) lacked antimetastatic activity. The results further support the role of activated macrophages in the destruction of M109 micrometastases.

L25 ANSWER 12 OF 33 MEDLINE
ACCESSION NUMBER: 84117830 MEDLINE
DOCUMENT NUMBER: 84117830 PubMed ID: 6363969
TITLE: Immunohistochemical and neurochemical evidence for the presence of serotonin in the adrenal medulla of the rat.
AUTHOR: Verhofstad A A; Jonsson G
SOURCE: NEUROSCIENCE, (1983 Dec) 10 (4) 1443-53.
Journal code: NZR; 7605074. ISSN: 0306-4522.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198403
ENTRY DATE: Entered STN: 19900319
Last Updated on STN: 19970203
Entered Medline: 19840323

AB Immunohistochemical and biochemical techniques were used to look for serotonin in the adrenal medulla of the rat. Using antibodies to serotonin, noradrenaline and adrenaline, it could be shown that the adrenaline-storing cells are highly immunoreactive for serotonin. Noradrenaline-storing cells were not stained even after **administration** of the precursors L-tryptophan and 5-hydroxytryptophan, or of serotonin itself. Specificity of the immune reaction was studied by both absorption and inhibition experiments. Chemical assays showed that rat adrenals contain significant amounts of serotonin (1.4 +/- 0.11 micrograms/g wet weight) which is about 0.4% of the adrenaline levels. Serotonin could be reduced to about 10% of control by a high dose of reserpine. From differential and sucrose gradient centrifugation experiments it was concluded that serotonin is probably stored in granules also containing adrenaline. **Administration** of 5-hydroxytryptophan led to a marked increase of the serotonin level, preferentially in the granular fraction. This increase could be blocked almost completely by a decarboxylase inhibitor. Serotonin **administration** did not result in a statistically significant increase of the serotonin concentration. Serotonin levels were not changed either after **administration** of L-tryptophan or the tryptophan hydroxylase inhibitor **H22**/54. These results indicate that there is no significant synthesis of serotonin from L-tryptophan. It is suggested that the serotonin present in the adrenaline-storing cells is derived from circulating serotonin and/or 5-hydroxytryptophan. Serotonin taken up directly from the circulation or formed by decarboxylation from 5-hydroxytryptophan is subsequently incorporated in the chromaffin granules.

L25 ANSWER 13 OF 33 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:894255 CAPLUS
TITLE: Experimental studies of antitumor effect of artesunate on liver cancer
AUTHOR(S): Wang, Qin; Wu, Limao; Li, Aiyuan; Zhao, Yi; Wang, Naiping
CORPORATE SOURCE: Guangxi Traditional Chinese Medical University, Nanning, 530001, Peop. Rep. China
SOURCE: Zhongguo Zhongyao Zazhi (2001), 26(10), 707-708, 720
CODEN: ZZZAE3; ISSN: 1001-5302
PUBLISHER: Zhongguo Yaoxuehui
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The inhibitory effect of artesunate on liver cancer in vitro and in vivo was studied. The mice bearing **H22** solid or ascitic liver tumor were applied in vivo expts. Me thiazolyl tetrazolium (MTT) assay and colony-forming unit assay were applied to test the cytotoxicity to human hepatocarcinoma SMMC-7721 cell line in vitro. The growth of solid tumor was obviously inhibited by artesunate at the dose of 300 mg kg-1 d-1 ig for 7 days. The tumor inhibiting rate of artesunate was 49.1%, 48.7%, 46.6% in 3 expts., resp. After **administration** of artesunate, the survival rate of the mice bearing **H22** ascitic liver tumor increased to 45%. Compared with the control groups, the difference was statistically significant (P <0.01). In addnl., artesunate could synergize the antitumor activity of 5-fluorouracil. Artesunate showed evident cytotoxicity to human hepatocarcinoma SMMC-7721 cells, the IC50 of artesunate was 2.07 .mu.g mL-4 in MTT expt. and 2.48 .mu.g ml-1 in colony-forming unit expt. Artesunate had marked antitumor activity in vitro and in vivo.

L25 ANSWER 14 OF 33 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:893765 CAPLUS
TITLE: Effect of APBMV on tumor weight and lipid peroxidation of H22-bearing mice after radiotherapy
AUTHOR(S): Wei, Ling; Dong, Weihua; Kong, Tianhan; Han, Xuefei; Chen, Huayan; Yang, Zhihua; Ju, Jihang; Guo, Jinwu
CORPORATE SOURCE: Center of Venom and Biological Toxins, Henan Medical University, Zhengzhou, 450052, Peop. Rep. China
SOURCE: Henan Yike Daxue Xuebao (2001), 36(6), 655-658
CODEN: HEYDE2; ISSN: 1000-1069
PUBLISHER: Henan Yike Daxue Xuebao Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The effects of antineoplastic polypeptide from Buthus martensii venom (APBMV) combined with radiotherapy (RT) on tumor wt. and lipid peroxidn. of hepatoma 22 (**H22**)-bearing mice were studied. One hundred **H22**-bearing mice were used, and tumor growth inhibition rate (IR), activity of superoxide dismutase (SOD), and level of lipid peroxide (LPO) were detected as the parameters. After RT or **administration** of different dosage of APBMV combined with RT, the changes of these parameters were obsd. On the 6th and 9th d after radiotherapy, the tumor wt. was decreased after **administrating** APBMV combined with RT, and IR was 78.28% and 70.45%, resp. as compared with RT and APBMV groups (P <0.05 or 0.01). SOD activity was the lowest and LPO level was the highest in RT group as compared with control group (P <0.05). SOD activity was increased and LPO level was decreased evidently in high dosage of APBMV with RT group as compared with those in RT group (P <0.01) and approached the levels of the control groups. The results showed that the inhibition effect of the combining therapy (APBMV combining with RT) on **H22** was stronger than radiation or APBMV alone, and APBMV can resist lipid peroxidn. injury induced by radiation in **H22** -bearing mice.

L25 ANSWER 15 OF 33 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:606485 CAPLUS
TITLE: Inhibition of proliferation and expression of N-ras in hepatoma cell by antioxidation treatment
AUTHOR(S): Liu, Shanlin; Shi, Dongyun; Pan, Xihua; Shen, Zonghou
CORPORATE SOURCE: Department of Biochemistry, Medical Center of Fudan University, Shanghai, 200032, Peop. Rep. China
SOURCE: Shengwu Huaxue Yu Shengwu Wuli Xuebao (2001), 33(4), 463-466
CODEN: SHWPAU; ISSN: 0582-9879
PUBLISHER: Shanghai Kexue Jishu Chubanshe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The inhibition of proliferation and expression of N-ras in hepatoma cell by antioxidn. treatment were studied. Kunming mice inoculated with hepatoma cell (**H22**) suspension s.c. at their right axilla were **administered** orally with antioxidants including vitamin E, .beta.-carotene, glutamine, kappa- selenocarrageenan and polysaccharide-peptide of coriolus (PSP) soln. It was found that the inoculated hepatoma growth was suppressed to various extents. The two kinds of polysaccharide antioxidants improved non- specific immunity, enhanced the nitrogen monoxide (NO) content in plasma and strengthened the inhibition of hepatoma. Above antioxidants added in the culture of 7721 human hepatoma cells inhibited the cell proliferation and induced its apoptosis. Meanwhile, the activity of glutathione peroxidase (GSH-Px) in the plasma of mice increased and the content of malondialdehyde decreased. H2O2 in low concn. improved the cancer cell proliferation and enhanced the expression of Mn-SOD, c-fos and c- jun, but led to cells apoptosis or necrosis in high concn. The mechanism of antioxidants inhibiting tumor growth and improving cancer cells apoptosis might be that, on the one hand, the antioxidants blocked the free radicals signal transduction on cancer cells proliferation, and on the other hand, they improved the release of NO through enhancing the non-specific immunity, so inhibiting the cancer cells proliferation directly.

L25 ANSWER 16 OF 33 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:6710 CAPLUS
DOCUMENT NUMBER: 135:86635
TITLE: Primary observation on effect of APBMV on tumor weight and general physical condition of hepatoma 22-bearing mice after radiotherapy.
AUTHOR(S): Kong, Tianhan; Wei, Ling; Han, Xuefei; Dong, Weihua
CORPORATE SOURCE: Center of Venom and Biological Toxins, Henan Medical University, Zhengzhou, 450052, Peop. Rep. China
SOURCE: Zhonghua Fangshe Yixue Yu Fanghu Zazhi (2000), 20(5), 313-316
CODEN: ZFYZDY; ISSN: 0254-5098
PUBLISHER: Weishengbu Gongye Weisheng Shiyanso
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The effect of antineoplastic polypeptide from Buthus martensii venom

(APBMV) combined with radiotherapy on hepatoma-bearing mice was studied. Hundreds of **H22**-bearing mice were used in this expt. The tumor growth inhibiting rate (IR%), WBC (white blood cell) count, Hb content, activity of superoxide dismutase (SOD), level of lipid peroxide (LPO) and spleens index (SI) were used as the parameters. The changes of these parameters were obsd. after radiotherapy (RT) or after **administration** of different dosage of APBMV combined with RT. The tumor wts. decreased after **administering** APBMV combined with RT, in which IR were 78.29% and 70.45%, resp. on the 6th and 9th day after radiotherapy. WBC count and SI were also higher than those of the RT group in RT + APBMV group. Measurement of Hb content in peripheral blood indicated that there were no differences ($P > 0.05$) among all groups. SOD activity was the lowest and LPO level was the highest in RT group (compared with the control group, $P < 0.05$, $P < 0.01$). SOD activity increased and LPO level decreased evidently and approached the levels of the control group'combining the high dosage of APBMV with RT to treat **H22**-bearing mice. The inhibiting effect of the combination therapy (APBMV combining with RT) on **H22** was stronger than radiation or APBMV alone. APBMV can also antagonize radiation injury on **H22**-bearing mice.

L25 ANSWER 17 OF 33 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:654178 CAPLUS
DOCUMENT NUMBER: 134:65890
TITLE: Inhibitory effect of antineoplastic polypeptide-III (AP-III) from Buthus martensii venom on transplanting hepatoma-22 and influence of AP-III on thymus gland weight of tumor-bearing mice
AUTHOR(S): Han, Xuefei; Wang, Yongkui; Chen, Huayan; Guo, Jinwu; Dong, Weihua; Kong, Tianhan
CORPORATE SOURCE: Center of Venom and Biological Toxins, Henan Medical University, Zhengzhou, 450052, Peop. Rep. China
SOURCE: Henan Yike Daxue Xuebao (2000), 35(4), 288-290
CODEN: HEYDE2; ISSN: 1000-1069
PUBLISHER: Henan Yike Daxue Xuebao Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB Aim: To observe the inhibitory effect of antineoplastic polypeptide-III from APBMV, antineoplastic polypeptide from Buthus martensii venom, (AP-III) on mouse hepatoma-22 (**H22**)and influence of AP-III on thymus gland wt. of tumor-bearing mice. Methods: Sixty-five mice were inoculated by **H22** cells and 24 h later were divided into 5 groups: 10 for 5-Fu group (20 mg/kg), 10 for APBMV group (0.04 mg/kg), 10 for AP-III group-I (0.04 mg/kg), 10 for AP-III group-II(0.03 mg/kg) and 25 for non-normal control group(saline). The mice were **administered** by i.p. injection once a day for 10 days and then killed. The wt. changes of tumor and thymus gland were obsd. accurately and statistically. Results: Growth of **H22** was inhibited markedly by AP-III at two dosages used in this expt. and APBMV, compared with non-normal control group, the differences were significant ($P < 0.01$ or $P < 0.001$), and indexes of thymus gland were lower in 5-Fu group and higher or similar in two AP-III and APBMV groups. Conclusion: Growth of **H22** was efficiently inhibited by AP-III. The thymus gland wt. of **H22** -bearing mice was increased by high dosage of AP-III.

L25 ANSWER 18 OF 33 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:304489 CAPLUS
DOCUMENT NUMBER: 133:187712
TITLE: Inhibitive effect of antineoplastic polypeptide from Buthus martensii venom on liver neoplasms
AUTHOR(S): Dong, Wei-hua; Han, Xue-fei; Wei, Ling; Kong, Tian-han
CORPORATE SOURCE: Center of Venom and Biological Toxins, Henan Medical University, Zhengzhou, 450052, Peop. Rep. China
SOURCE: Zhongguo Bingli Shengli Zazhi (2000), 16(2), 123-127
CODEN: ZBSZEB; ISSN: 1000-4718
PUBLISHER: Jinan Daxue
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB AIM: To observe the growth inhibiting effect of antineoplastic polypeptide from Butbhus Martensii venom (APBMV) on liver neoplasm. RESULTS: Following the **administration** of APBMV, the ability of SMMC-7721 cells to metabolize MTT was significantly lower than was obsd. in untreated control cells. The IC50 of APBMV was 11.3 .mu.g/mL. The growth of SMMC-7721 cells was significantly inhibited by APBMV and a dose-response relationship was clear; the IC50 were 15.87 .mu.g/mL, 13.05 .mu.g/mL and 8.70 .mu.g/mL resp. With of APBMV > 8 .mu.g/mL, the colony formation rate of SMMC-7721 cells was also decreased significantly compared with controls. Tumor growth of **H22**-bearing mice was inhibited by APBMV, the growth inhibiting rate was 37.31 % ($P < 0.01$); after treatment with APBMV, white blood cell(WBC) count and spleen index of **H22**-bearing mice were not changed markedly or slightly higher than those obsd. in the control group. In 5-fluorouracil treated group, WBC count and spleen index of **H22** bearing mice were all significantly reduced ($P < 0.01$). CONCLUSION: APBMV was one kind of effective and low toxicity antineoplastic components in the venom of Buthus martensii scorpion. It possesses antineoplastic activity on SMMC-7721 and **H22** hepatoma cells.

L25 ANSWER 19 OF 33 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:248767 CAPLUS
DOCUMENT NUMBER: 133:202707
TITLE: Antitumor effect of shark cartilage
AUTHOR(S): Yi, Meihua; Zhang, Lishi
CORPORATE SOURCE: Hainan University, Haikou, 570228, Peop. Rep. China
SOURCE: Zhongguo Haiyang Yaowu (2000), 19(1), 36-37, 50
CODEN: ZHYAE8; ISSN: 1002-3461
PUBLISHER: Shandongsheng Haiyang Yaowu Kexue Yanjiuso
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The antitumor effect of shark (Cetorhinus maximus) cartilage capsules was studied. Mice bearing **H22** hepatoma and S180 sarcoma were used, and capsules of shark cartilage were **administered** orally at 1.0, 2.0 and 3.0 g/kg. The shark cartilage capsules significantly decreased the tumor wts.

L25 ANSWER 20 OF 33 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:289340 CAPLUS
DOCUMENT NUMBER: 131:69538
TITLE: Influence of antineoplastic polypeptide from Buthus martensii venom on immune system function of hepatoma H22-bearing mice
AUTHOR(S): Dong, Weihua; Kong, Tianhan; Lei, Liugen; Han, Xuefei; Wang, Chengyu; Yang, Jianbing; Zheng, Xiangyu; Cheng,

Huayan
CORPORATE SOURCE: Center of Venom and Biological Toxins, Henan Medical University, Zhengzhou, 450052, Peop. Rep. China
SOURCE: Henan Yike Daxue Xuebao (1999), 34(1), 67-70
CODEN: HEYDE2; ISSN: 1000-1069
PUBLISHER: Henan Yike Daxue Xuebao Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The influence of antineoplastic polypeptide from Buthus martensii venom (APBMV) on NK activity, WBC of peripheral blood, lymphocyte blastogenesis, delayed type hypersensitivity (DTH) response and hemolysin levels in hepatoma **H22**-bearing mice were obsd. The mice inoculated by hepatoma **H22** cells for 24 h were divided into 4 groups of 10 mice each. Mice in control group were i.p. given saline. Mice were i.p. injected 5-Fu at 10 mg.cntdot.kg-1 in 5-Fu treated group. In APBMV treated group, mice were i.p. **administered** APBMV 0.03 mg.cntdot.kg-1. In combined APBMV with 5-Fu (APBMV+5-Fu) group, mice were i.p. **administered** APBMV (0.03 mg.cntdot.kg-1) and 5-Fu (10 mg.cntdot.kg-1) together. All chems. were given to mice for 5 days. The changes of indexes mentioned above of **H22** carrying mice were obsd. after treatments. NK cells activity and response of DHT induced by DNCB in **H22** carrying mice enhanced remarkably and proliferating index of lymphocyte activated by ConA increased evidently in both APBMV and APBMV+5-Fu groups. Compared with control and 5-Fu groups there were significant differences ($P < 0.05$ or $P < 0.01$ or $P < 0.001$). WBC no. of **H22**-bearing mice treated with APBMV alone increased markedly compared with control ($P < 0.01$). WBC count decreased markedly ($P < 0.01$) in the mice treated with 5-Fu compared with control, but in APBMV+5-Fu group, WBC count increased approaching the control level. The difference of WBC count between APBMV + 5-Fu and 5-Fu groups was significant ($P < 0.05$). APBMV could also enhance the hemolysin level of peripheral blood in **H22**-bearing mice ($P < 0.05$). APBMV can antagonize or recover the immunity inhibition or defect induced by chem. drugs or the tumor.

L25 ANSWER 21 OF 33 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:289338 CAPLUS
DOCUMENT NUMBER: 131:82680
TITLE: Inhibitory effect of antineoplastic polypeptide from Buthus martensii venom on transplanting tumors
AUTHOR(S): Dong, Weihua; Kong, Tianhan; Wang, Chengyu; Lei, Luigen; Han, Xuefei; Wei, Ling; Wang, Yongkui; Zheng, Xianyu; Wu, Yiming
CORPORATE SOURCE: Center of Venom and Biological Toxins, Henan Medical University, Zhengzhou, 450052, Peop. Rep. China
SOURCE: Henan Yike Daxue Xuebao (1999), 34(1), 61-63
CODEN: HEYDE2; ISSN: 1000-1069
PUBLISHER: Henan Yike Daxue Xuebao Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB To observe the inhibitory effect of antineoplastic polypeptide from Buthus martensii venom (APBMV) on transplanting tumors-hepatoma 22(**H22**) and melanoma B16. Tumor wt., tumor growth inhibitory rate (IR%), WBC count in peripheral blood and spleen index (SI) were detd. in tumor-bearing mice. Mice were inoculated by **H22** and B16, and 24 h later, and the tumor-bearing mice were divided into control, 5-Fu-treated and the APBMV-treated groups. The mice in APBMV-treated group were **administered** 0.03 mg.cntdot.kg-1, 0.04 mg.cntdot.kg-1 and 0.06 mg.cntdot.kg-1 of APBMV sep. by i.p. injection. 5-Fu-treated and control group were given 20 mg.cntdot.kg-1 of 5-Fu and equal vol. saline, resp. Tumor-bearing mice were killed after the chems. were given for 10 days. Growth of **H22** was inhibited markedly by APBMV at three doses used in this test. Inhibitory rate was over 30% compared with control group and there was a significant difference ($P < 0.001$). B16 growth was inhibited by two high doses of APBMV, inhibitory rates were 40.36% and 44.58% resp. Inhibitory effect of APBMV on B16 was stronger than that of 5-Fu (33.55%). Compared with control, WBC count and SI of **H22** bearing mice were reduced notably. There were significant differences between 5-Fu, control, and APBMV-treated groups ($P < 0.001$). The growth of **H22** and B16 tumors was efficiently inhibited by APBMV.

L25 ANSWER 22 OF 33 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:707995 CAPLUS
DOCUMENT NUMBER: 130:162795
TITLE: Experimental study on antitumor effect of germanium citrate
AUTHOR(S): Lu, Sulin; Zhang, Guilin; Zhong, Hengliang; Ren, Guangyou
CORPORATE SOURCE: Guiyang Medical College, Guiyang, 550004, Peop. Rep. China
SOURCE: Guangdong Weiliang Yuansu Kexue (1998), 5(7), 44-46
CODEN: GWYKF3; ISSN: 1006-446X
PUBLISHER: Guangdong Weiliang Yuansu Kexue Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The antitumor effect of Ge citrate on transplanted tumor sarcoma180, **H22**, and P388 in mice was studied. Ge citrate was **administered** orally to mice at 0.2 g/kg and 0.4 g/kg, resp. The av. inhibitory rates to sarcoma180 were 47.62% and 52.38%, those of Hep22 were 46.15% and 52.20%, and the prolonging rates of the survival time to P388 were 24.42% and 30.18%, resp. The results showed that Ge citrate had antitumor effect.

L25 ANSWER 23 OF 33 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:7314 CAPLUS
DOCUMENT NUMBER: 128:70419
TITLE: Antitumor efficacy of adriamycin encapsulated in liposomes in mice
AUTHOR(S): Qi, Xianrong; Xiao, Yu; Wei, Shuli; Cui, Jingrong; Xu, Bo
CORPORATE SOURCE: Sch. Pharmaceutical Sci., Beijing Med. Univ., Beijing, 100083, Peop. Rep. China
SOURCE: Zhongguo Yaoxue Zazhi (Beijing) (1997), 32(4), 207-210
CODEN: ZYZAEU; ISSN: 1001-2494
PUBLISHER: Zhongguo Yaoxuehui
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The antitumor activity of adriamycin-liposomes (Adrliposomes) against **H22** and S180 tumor in mice was studied. Adr was encapsulated in dipalmitoylphosphatidylcholine (DPPC) and soybean-derived sterol (SS) and PEG-DSPE liposomes (DPPC/SS liposomes and DPPC/SS/PEG-liposomes). The 2 liposomes and free Adr were **administered** in the tail vein of **H22** and S180 tumor-bearing mice. The antitumor efficacy of Adr

encapsulated in DPPC/SS-liposomes and DPPC/SS/PEG-liposomes was higher than that of the free drug and DPPC/SS/PEG-liposome was markedly active. The results suggest that liposomes delivery Adr may provide antitumor activity against **H22** and S180 cancer.

L25 ANSWER 24 OF 33 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:628813 CAPLUS
DOCUMENT NUMBER: 127:273093
TITLE: Experimental study on immunomodulation and antitumor effects of melatonin in H22 hepatoma-bearing mice
AUTHOR(S): Jianjun, Yan; Feng, Shen; Mengchao, Wu
CORPORATE SOURCE: Eastern Hepatobiliary Surgery Hospital, Second MilitaryMedical University, Shanghai, 200433, Peop. Rep. China
SOURCE: J. Med. Coll. PLA (1997), 12(2), 132-135
CODEN: JMCPE6; ISSN: 1000-1948
PUBLISHER: Journal of Medical Colleges of PLA, Editorial Board
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Studies were carried out to observe immunomodulation and antitumor effect of melatonin (MLT) in tumor-bearing mice. By flow cytometry and MTT colorimetry, the immunol. indexes of **H22** hepatoma-bearing mice were investigated. MLT **administration** could increase the CD4+/CD8+ cell ratio in the peripheral blood of the tumor-bearing mice, cooperate with IL-2 to promote the proliferation of lymphocytes and eosinophils, increase NK and LAK activity of splenocytes, and enhance the prodn. of IL-2 from splenocytes. The authors also found that MLT could inhibit tumor growth and prolong the survival time of the tumor-bearing mice in vivo. Moreover, a synergetic effect of IL-2 and MLT was obsd. It seems that MLT had no effect on **H22** hepatoma cell growth in vitro. It is suggested that MLT may be a potential candidate for tumor immunotherapy as one of the biol. reaction modulators (BRM).

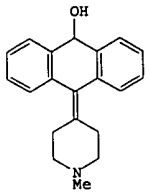
L25 ANSWER 25 OF 33 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:671570 CAPLUS
DOCUMENT NUMBER: 125:316478
TITLE: Antitumor effect of alkaline soluble proteolycan extracted from Hohenbuehelia serotina (Schard, Fr.) Sing.
AUTHOR(S): Cao, Ruimin; Zhao, Zhongwei; Ye, Fei; Su, Zhijie
CORPORATE SOURCE: School of Basic Medical Sciences, Norman Bethune University of Medical Sciences, Changchun, 130021, Peop. Rep. China
SOURCE: Zhongguo Zhongyao Zazhi (1996), 21(6), 372
CODEN: ZZZAE3; ISSN: 1001-5302
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The death rate (at 60th day) of mice treated with alk. sol. proteolycan was obviously lower than untreated control group, 3/8 vs 8/8, $P < 0.001$; tumor tissue size (at 30th day) in treated group was obviously lower than control group, 9.33 .+-. 5.7 vs 46.22 .+-. 24.3 cm3, $P < 0.001$. In liver cancer bearing **H22** mice, lung tissue mass wt. of mice treated with the proteolycan was obviously lower than that in mice untreated control group, 0.88 .+-. 0.61 vs 2.5 .+-. 0.92 g, 10 days after **administration** of the protein glycan. The results suggest that alk. sol. proteolycan has antitumor effect.

L25 ANSWER 26 OF 33 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:485569 CAPLUS
DOCUMENT NUMBER: 119:85569
TITLE: Immuno-tumoricidal effect of Rehmannia glutinosa polysaccharide b and its mechanism
AUTHOR(S): Chen, Lizhen; Feng, Xingwan; Zhou, Jinhuang; Tang, Jianfang
CORPORATE SOURCE: Inst. Pharmacol. Toxicol., Acad. Mil. Med. Sci., Beijing, 100850, Peop. Rep. China
SOURCE: Zhongguo Yaolixue Yu Dulixue Zazhi (1993), 7(2), 153-6
CODEN: ZYYZEW; ISSN: 1000-3002
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The polysaccharide fraction, Rehmannia glutinosa polysaccharide b (RPS-b) was found to inhibit the growth of solid tumors S180, Lewis, B16, and **H22** in mice by i.p. 20-40 mg.cntdot.kg-1 daily for 8 days since the second day of tumor transplantation. It was also effective by oral **administration** in expts. with S180. In vivo expts., RPS-b was ineffective in inhibiting the growth of S80 and HL60 cells. It showed a pos. immunomodulatory activity by a prolonged elevation of the proliferation of the splenic T lymphocytes. It could also partly block the inhibition of NK activity caused by tumor cell growth. These results demonstrate that RPS-b is an effective antitumor agent through its immuno-modulatory, particularly the cellular immune mechanism.

L25 ANSWER 27 OF 33 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1988:469587 CAPLUS
DOCUMENT NUMBER: 109:69587
TITLE: Treatment of H22 hepatoma transplanted in mice by radiotherapy and carcinophotorin PSD-007
AUTHOR(S): Wang, Fuan; Liu, Yanfang; Ding, Huaye; Chen, Dingyi
CORPORATE SOURCE: Dep. Pathol., 4th Mil. Med. Coll., Xian, Peop. Rep. China
SOURCE: J. Med. Coll. PLA (1987), 2(4), 323-7
CODEN: JMCPE6; ISSN: 1000-9094
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The radiosensitization of **H22** hepatomas transplanted into male Kunming strain mice by PSD-007 (20 .mu.g/g, i.p.) was studied when **administered** 10-12 h prior to x-irradn. PSD-007 alone had no effect on tumor growth. When used in combination with x-rays, marked tumor growth inhibition was obsd., with a sensitizer enhancement ratio of 1.44. The combined treatment caused more tumor cell injury and an earlier tumor-damaging response then that with x-rays alone. The membranous structures of tumor cells appear to be the target site of radiosensitization by PSD-007.

L25 ANSWER 28 OF 33 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1978:591110 CAPLUS
DOCUMENT NUMBER: 89:191110
TITLE: The influence of mianserin and danitracene, 5-hydroxytryptamine receptor blockers, on the 5-hydoxytryptamine disappearance induced by H22/54 in the rat brain
AUTHOR(S): Maj, J.; Mogilnicka, E.; Klimek, V.
CORPORATE SOURCE: Inst. Pharmacol., Pol. Acad. Sci., Krakow, Pol.

SOURCE: Pol. J. Pharmacol. Pharm. (1978), 30(2-3), 413-20
CODEN: PJPPAA
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Mianserin-HCl [21535-47-7] and danitracene (I) [31232-26-5] **administered** to rats did not change serotonin [50-67-9] but increased 5-hydroxyindoleacetic acid [54-16-0] levels in the brain 1 h after injection. Serotonin and 5-hydroxyindoleacetate levels were decreased at 24 h. Mianserin, I, and a comparative agent, cyproheptadine, accelerated the serotonin disappearance in pons and medulla regions when **administered** after **H22**/54, an inhibitor of serotonin synthesis. Mianserin also accelerated the serotonin depletion in the cortex. Thus, mianserin and I are antidepressants that accelerate serotonin depletion in some regions of rat brain.

L25 ANSWER 29 OF 33 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1968:409581 CAPLUS
DOCUMENT NUMBER: 69:9581
TITLE: Influence of cold exposure on catechol amine-depleting actions of hydroxylase inhibitors
AUTHOR(S): Chan, W. C.; Johnson, Gordon E.
CORPORATE SOURCE: Dep. Pharmacol., Univ. Toronto, Toronto, Can.
SOURCE: Eur. J. Pharmacol. (1968), 3(1), 40-6
CODEN: EJPHAZ
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The importance of catechol amine secretion in the cold was studied by treating rats placed at 27.degree. or 4.degree. with .alpha.-methyltyrosine (I), an inhibitor of tyrosine hydroxylase, .alpha.-propyl-(3,4-dihydroxyphenyl)acetamide (**H22**/54) (II), an inhibitor of tyrosine hydroxylase and phenylalanine hydroxylase, or .alpha.,.beta.,.beta.-trimethyl(3,4-dihydroxyphenyl)-alanine (trimethyldopa) (III), an inhibitor of phenylalanine hydroxylase. I and II were **administered** i.p. in doses of 80 mg./kg. to rats at 3-hr. intervals for 24 hrs. and III at 240 mg./kg. i.p. every 2 hrs. for 24 hrs. I produced the largest fall in tissue noradrenaline. II and III, although causing a moderate fall in noradrenaline stores at 27.degree., were more effective in the cold room. I and III depressed noradrenaline excretion and increased adrenaline release in the cold. The adrenaline served as a 2nd line of defense evoked by the noradrenaline decrease. Adrenodemedullated rats given I or II at 4.degree. showed a high rate of mortality. II lowered tissue and urinary levels of noradrenaline in the cold but failed to produce hypothermia and death in intact or adrenodemedullated rats. Other actions of II, such as inhibition of catechol-O-methyltransferase, may have contributed to the maintenance of normothermia. 19 references.

L25 ANSWER 30 OF 33 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1966:87484 CAPLUS
DOCUMENT NUMBER: 64:87484
ORIGINAL REFERENCE NO.: 64:16497f-g
TITLE: Blockade of the psychotic syndrome caused by nialamide in mice
AUTHOR(S): Corrodi, H.
CORPORATE SOURCE: AB Hassle, Res. Labs., Goteborg, Swed.
SOURCE: J. Pharm. Pharmacol. (1966), 18(3), 197-9
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Intraperitoneal injection of 500 mg. .alpha.-propyl-3,4-dihydroxyphenylacetamide/kg. (**H22**/54) or 500 mg. L-.alpha.-methyldopa/kg. 3 hrs. after the **administration** of 500 mg. nialamide/kg. to male mice blocked the psychotic syndrome in the animals. DL-.alpha.-Methyltyrosine Me ester (500 mg./kg.), which inhibits the synthesis of dopamine and noradrenaline, did not inhibit the psychotic syndrome. Since the psychotic syndrome caused by the injection of nialamide is accompanied by a large increase in the level of 5-hydroxytryptamine in the brain, **H22**/54 and L-.alpha.-methyldopa, which inhibit the synthesis of noradrenaline and 5-hydroxytryptamine almost completely, blocked the development of the psychotic syndrome by inhibiting the formation of 5-hydroxytryptamine. The high level of 5-hydroxytryptamine in mouse brain after treatment with nialamide may be responsible for this model psychosis.

L25 ANSWER 31 OF 33 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96274955 EMBASE
DOCUMENT NUMBER: 1996274955
TITLE: Effects of 8-chloroadenosine on murine hepatoma H22 cells.
AUTHOR: Zhan J.-H.; Fang J.-C.; Shi Y.-J.; Peng J.; Wang D.-S.; Liang Y.-Y.
CORPORATE SOURCE: Beijing Inst. for Cancer Research,Beijing 100034, China
SOURCE: Chinese Pharmacological Bulletin, (1996) 12/1 (71-73).
ISSN: 1001-1978 CODEN: ZYTOE8
COUNTRY: China
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
022 Human Genetics
029 Clinical Biochemistry
048 Gastroenterology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: Chinese
SUMMARY LANGUAGE: Chinese; English

AB 8-Chloroadenosine showed marked activity against murine hepatoma **H22** solid tumor, at 100 mg.cntdot.kg-1.cntdot.d-1 x 7 d. The inhibition rates of **H22** were 71.3 .+-. 13.3% (P<0.01) and 66.1 .+-. 4.46% (P<0.01) by ip. and iv. **administration** respectively.

8-Cl-Ado increased intercellular cAMP concentration but decreased diacylglycerol amount in **H22** ascites cells. Photoaffinity labeling/SDS-polyacrylamide gel electrophoresis assay indicated that 8-Cl-Ado greatly decreased R I (regulatory subunit of PKA) in the cytosol of **H22** cells. Gel retardation analysis demonstrated the enhancement of CRE-binding activity after treatment for 24 hours with 8-Cl-Ado. Using in situ hybridization, 8-Cl-Ado induced antioncogene p 53 expression.

L25 ANSWER 32 OF 33 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 83039753 EMBASE
DOCUMENT NUMBER: 1983039753
TITLE: 8-Hydroxy-2-(di-n-propylamino)tetralin, 8-OH-DPAT, a potent and selective simplified ergot congener with central 5-HT-receptor stimulating activity.
AUTHOR: Hjorth S.; Carlsson A.; Lindberg P.; et al.
CORPORATE SOURCE: Dep. Pharmacol., Univ. Goteborg, Goteborg, Sweden
SOURCE: Journal of Neural Transmission - General Section, (1982) 55/3 (169-188).
CODEN: JNTMAH
COUNTRY: Austria
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
002 Physiology
008 Neurology and Neurosurgery
030 Pharmacology
LANGUAGE: English
AB It was demonstrated that the simplified ergot congener 8-hydroxy-2-(di-n-propylamino)tetralin, 8-OH-DPAT, is able to elicit pronounced biochemical and behavioural alterations indicative of central serotoninomimetic activity. Since these effects are resistant to prior monoamine depletion and/or synthesis inhibition by means of reserpine and .alpha.-propyldopacetamide (**H22**/54), respectively, they are most likely to be attributable to direct serotonin-receptor agonism by 8-OH-DPAT. With regard to central 5-HT neurotransmission the effects of 8-OH-DPAT - 5-HT levels, decreased 5-HIAA levels, 5-HT-synthesis rate and 5-HT utilization and inhibited 5-HT neuronal firing - are virtually identical, and comparable in potency, to those reported to result from the **administration** of lisuride or LSD. In contrast, however, to lisuride and LSD (included for comparative purposes in this study) as well as to several differently N-substituted, 5,6-dihydroxy, 6,7-dihydroxy and 5-, 6- and 7-monohydroxy 2-aminotetralins, 8-OH-DPAT lacks appreciable effects on central catecholamine receptors. The compound may thus be regarded as the most potent, selective centrally acting 5-HT agonist described to date. In accordance with this it was shown that the full-blown 5-HT-like behavioural syndrome induced by 8-OH-DPAT cannot be antagonized by reserpine, phenoxybenzamine, propranolol and haloperidol. In addition, of the three putative 5-HT-receptor blockers cyproheptadine, methergoline and methiothepin only the latter was able to counteract the 8-OH-DPAT-induced syndrome. The results are discussed in relation to the recent subclassification of central 5-HT receptor sites. A comparison between the chemical structures and biological activities for different fragments of the ergot nucleus was also made. The data suggest that while the role of the A ring in the ergot structure for dopaminergic activity at present is unclear, this ring may be important for the 5-HT activity like in e.g. lisuride and LSD. Moreover, based on the present results and literature reports, it is speculated that a selective 5-HT-receptor agonist such as 8-OH-DPAT would not be liable to induce hallucinations in man.

L25 ANSWER 33 OF 33 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 80084012 EMBASE
DOCUMENT NUMBER: 1980084012
TITLE: [Antimalarial chemotherapy in tropical Africa]. RECOURS AUX MEDICAMENTS POUR LA LUTTE ANTIPALUDIQUE EN AFRIQUE TROPICALE.
AUTHOR: Kouznetsov R.
CORPORATE SOURCE: Programme Action Antipaludique, Organ. Mondiale Sante, 1211 Geneve 27, Switzerland
SOURCE: Bulletin of the World Health Organization, (1979) 57/5 (691-696).
CODEN: BWHOA6
COUNTRY: Switzerland
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
017 Public Health, Social Medicine and Epidemiology
004 Microbiology
LANGUAGE: French
AB At present in the countries of tropical Africa chemotherapy is the main, and often the only, practical method of combatting malaria from the operational, **administrative** and financial point of view. This is particularly so in rural zones. The present article reviews the experience which has been acquired in chemotherapy in Africa since the end of the 1940's with C23 H30 CIN30, with C11 H16 CIN5, with C12 H13 CIN4, with C18 H26 CIN3, with C20 **H22** CIN30, as well as with sulfones and sulfamides in combination with the inhibitors of dihydrofolate reductase. C18 H26 CIN3 has proved to be the most effective and has therefore become the chosen drug whenever malarial parasites are prevalent. Since reports have indicated the presence in Eastern Africa of stubs of Plasmodium falciparum, which resist amino-4 quinolin, it is essential to establish national and regional policies which promote national use of anti-malarial drugs. In most African countries activity is still limited to the **administration** to patients of anti-malarial drugs by means of a restricted network of health institutions. In certain countries however, attempts have been made to extend the chemotherapeutic treatment by mobilising benevolent collaborators, or **administering** chemosuppressive treatment to vulnerable groups in the population (infants, young children, pupils, pregnant women, and mothers of infants). But the effectiveness of these methods depends obviously on the degree of commitment of the benevolent collaborators, the health officials and the communities themselves.

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(FILE 'HOME' ENTERED AT 09:36:34 ON 05 APR 2002)

FILE 'MEDLINE, CAPLUS, EMBASE' ENTERED AT 09:36:54 ON 05 APR 2002
L1 7 S FCGAMMAR1
L2 65 S FC (1N) GAMMA (1N) R1
L3 1957 S FC (1N) GAMMA (1N) RI
L4 982 S CD64
L5 0 S L1 AND L2 AND L3 AND L4

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L6          2547 S L1 OR L2 OR L3 OR L4
L7          1130 S L6 (P) ANTIBOD?
L8            54 S L7 (P) ADMINIST?
L9            26 DUP REM L8 (28 DUPLICATES REMOVED)
L10          585 S VAN DE WINKEL?/AU
L11         1074 S L10 AND MACROPHAGE? OR CD64
L12          183 S L10 AND (MACROPHAGE? OR CD64)
L13          127 S L12 (P) ANTIBOD?
L14           11 S L13 (P) ADMINIST?
L15            7 DUP REM L14 (4 DUPLICATES REMOVED)
L16          299 S L4 (P) MACROPHAGE?
L17            0 S L16 AND PSORIASIS
L18           10 S L16 AND (HIV)
L19            5 DUP REM L18 (5 DUPLICATES REMOVED)
L20           23 S L16 AND (LUPUS OR SCLERODERMA OR DERMATITIS OR WEGENER? OR RA
L21           12 DUP REM L20 (11 DUPLICATES REMOVED)
L22          816 S (MAB (1N) 22) OR H22 OR (CRL (1N) 1117)
L23           58 S L22 (P) ADMINIST?
L24           35 DUP REM L23 (23 DUPLICATES REMOVED)
L25           33 S L24  NOT L7

=> s cl2mdp
L26          458 CL2MDP

=> s l26 (10N) antibod?
L27           10 L26 (10N) ANTIBOD?

=> dup rem 27
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=> dup rem l27
PROCESSING COMPLETED FOR L27
L28            5 DUP REM L27 (5 DUPLICATES REMOVED)

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L28  ANSWER 1 OF 5      MEDLINE
ACCESSION NUMBER:    1999002354      MEDLINE
DOCUMENT NUMBER:     99002354   PubMed ID: 9788305
TITLE:               Cytotoxic T lymphocytes and antibodies after orthotropic
                     penetrating keratoplasty in rats treated with
                     dichloromethylene diphosphonate encapsulated liposomes.
AUTHOR:              Van der Veen G; Broersma L; Van Rooijen N; Van Rij G; Van
                     der Gaag R
CORPORATE SOURCE:    Department of Ophthalmo-Immunology, The Netherlands
                     Ophthalmic Research Institute, Amsterdam.
SOURCE:              CURRENT EYE RESEARCH, (1998 Oct) 17 (10) 1018-26.
                     Journal code: DUB; 8104312. ISSN: 0271-3683.
PUB. COUNTRY:        ENGLAND: United Kingdom
                     Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         199812
ENTRY DATE:          Entered STN: 19990115
                     Last Updated on STN: 19990115
                     Entered Medline: 19981208
AB   PURPOSE: To investigate the immunological basis for the prolonged corneal
     allograft survival after subconjunctival injections of liposomes filled
     with dichloromethylene diphosphonate (Cl2MDP-LIP). METHODS: F344 rats
     received orthotropic DA corneal grafts. One group of rats was treated with
     subconjunctival injections of Cl2MDP-LIP on days 0, 2, 4, 6 and 8
     postoperatively, the control groups received no treatment. Nineteen or 42
     days postoperatively cytotoxic T lymphocyte (CTL) activity was measured in
     the lymph nodes draining the grafted and the contralateral eyes, in the
     spleen and the mesenteric lymph nodes. Sera taken at the same time points
     were tested for presence of lytic alloantibodies. RESULTS: On day 19 CTL
     activity in submandibular lymph nodes draining the grafted eyes was
     similar in the 2 groups. In the mesenteric lymph nodes high CTL activity
     was found in the untreated rats and low in the Cl2MDP-LIP rats. The spleen
     showed high CTL activity in the untreated group but no activity in the
     liposome group. Forty two days postoperatively a decline in CTL activity
     was seen in both groups. Complement dependent anti-donor
     antibodies were absent in the Cl2MDP-LIP group at both
     time points whereas antibodies were present on days 19 and 42 in
     the untreated group. CONCLUSIONS: Repeated subconjunctival injection of
     Cl2MDP-LIP restricts the induction of cellular cytotoxicity against donor
     antigens to the regional lymph nodes and suppresses cytotoxic antibody
     formation.

L28  ANSWER 2 OF 5      MEDLINE                                  DUPLICATE 1
ACCESSION NUMBER:    1998103374      MEDLINE
DOCUMENT NUMBER:     98103374   PubMed ID: 9440200
TITLE:               The immune response to staphylococcal antigens in mice
                     depleted of macrophages by Cl2MDP-liposomes.
AUTHOR:              Rudnicka W; Wieckowska M; van Rooijen N; Rozalska B
CORPORATE SOURCE:    Department of Infectious Biology, Institute of Microbiology
                     and Immunology, University of Lodz, Poland.
SOURCE:              ZENTRALBLATT FUR BAKTERIOLOGIE, (1997 Nov) 286 (4) 511-22.
                     Journal code: BD7; 9203851. ISSN: 0934-8840.
PUB. COUNTRY:        GERMANY: Germany, Federal Republic of
                     Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         199803
ENTRY DATE:          Entered STN: 19980312
                     Last Updated on STN: 19980312
                     Entered Medline: 19980304
AB   To investigate the role of macrophages in the induction of the production
     of antibody to staphylococcal antigens, we used Cl2MDP
     (clodronate) liposomes as a tool for local macrophage depletion.
     Macrophage depletion caused in mice by intraperitoneal (i.p.) injection of
     Cl2MDP liposomes was associated with a reduction in the clearance of
     Staphylococcus aureus Cowan 1 bacteria from the tissues of infected
     animals and with a marked decrease in the bactericidal activity of
     macrophages escaping from the lethal effect of clodronate. Despite the
     functional defect of macrophages, the mice treated with Cl2MDP liposomes
     two days before the injection of alpha-toxin (toxoid) or whole heat-killed
     S. aureus Cowan 1 bacteria, demonstrated an enhancement in the production
     of anti-staphylococcal alpha-toxin IgM and anti-collagen-binding protein
     IgG. A similar enhancement of antistaphylococcal antibody synthesis was
     observed in mice after receiving phosphate buffered saline (PBS)
     encapsulated in liposomes.
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L28 ANSWER 3 OF 5 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 94266567 MEDLINE
DOCUMENT NUMBER: 94266567 PubMed ID: 7911460
TITLE: The role of macrophages in the pathogenesis of HSV-1 induced chorioretinitis in BALB/c mice.
AUTHOR: Berra A; Rodriguez A; Heiligenhaus A; Pazos B; Van Rooijen N; Foster C S
CORPORATE SOURCE: Hilles Immunology Laboratory, Massachusetts Eye and Ear Infirmary, Harvard Medical School, Boston 02114.
CONTRACT NUMBER: EY06008 (NEI)
SOURCE: INVESTIGATIVE OPHTHALMOLOGY AND VISUAL SCIENCE, (1994 Jun) 35 (7) 2990-8.
Journal code: GWI; 7703701. ISSN: 0146-0404.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199407
ENTRY DATE: Entered STN: 19940721
Last Updated on STN: 19950206
Entered Medline: 19940711

AB PURPOSE. To examine the effects of modification of immune effector cells, including macrophages, in the pathogenesis of herpes simplex virus retinitis in BALB/c mice. METHODS. Two intravitreal injections (2 microliters each) of anti-CD11b monoclonal antibody (mAb) [13 micrograms/microliters] were administered to the contralateral eyes of 10 BALB/c mice on days 6 and 8 after HSV inoculation into the right anterior chamber (AC) with HSV-1. A control group consisted of mice injected with anti-HLA-DR mAb in the same fashion. Specific macrophage depletion was performed in an additional group of 12 BALB/c mice by intravenous (i.v.) injection of dichloromethylene diphosphonate (Cl2MDP)-liposomes 7 days before AC HSV-1 inoculation into the eye. Control group consisted of mice receiving i.v. PBS-liposomes. Mice were clinically observed for 14 days postinfection, and the incidence of chorioretinal disease was confirmed by histopathologic studies. RESULTS. Intravitreal injections of anti-CD11b mAb produced a dramatic suppression of the contralateral retinal necrosis (2 of 10 mice) compared to 9 of 10 controls receiving an irrelevant **antibody** therapy ($P < 0.05$). Mice treated with i.v. **Cl2MDP** -liposomes also showed a significant inhibition of the development of contralateral chorioretinitis, with only 3 of 12 mice developing retinal disease compared to 9 of 12 mice from the control group ($P < 0.05$). FACS analysis performed on peripheral blood and spleen cells showed a significant depletion of Mac-1+ cells of Cl2MDP-liposome-treated but not of PBS-liposome-treated mice (controls). CONCLUSION. Intravitreal anti-CD11b mAb therapy, a broadly directed depletion strategy against many effector cells (macrophages, granulocytes, natural killer cells, and even cytotoxic T-cells) was most efficient in suppressing the HSV-1 induced contralateral disease. A more specific technique (i.v. Cl2MDP-liposome therapy) to deplete macrophages also produced a significant inhibition of HSV-1 induced contralateral chorioretinitis. These findings suggest that macrophages are important participants in the effector phase of the destructive inflammatory immune response induced by HSV-1 in the eye.

L28 ANSWER 4 OF 5 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 93328278 MEDLINE
DOCUMENT NUMBER: 93328278 PubMed ID: 8335357
TITLE: Binding of Candida albicans yeast cells to mouse popliteal lymph node tissue is mediated by macrophages.
AUTHOR: Han Y; van Rooijen N; Cutler J E
CORPORATE SOURCE: Department of Microbiology, Montana State University, Bozeman 59717.
CONTRACT NUMBER: AI24912 (NIAID)
SOURCE: INFECTION AND IMMUNITY, (1993 Aug) 61 (8) 3244-9.
Journal code: GO7; 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199308
ENTRY DATE: Entered STN: 19930903
Last Updated on STN: 19930903
Entered Medline: 19930826

AB We previously reported that Candida albicans yeast cells adhere to the macrophage-rich medullary and subcapsular sinus areas of mouse lymph node tissue. To determine whether the yeast cell-lymph node interaction is mediated by macrophages, the effect of specific elimination of macrophages on yeast cell binding was studied, and yeast cell adherence was correlated with the ingestion of India ink by lymph node cells. Macrophage elimination was done by use of liposome-containing dichloromethylene diphosphonate (L-Cl2MDP). Mice were injected in the hind footpads with the L-Cl2MDP preparation, popliteal lymph nodes were removed 5 days later, and yeast cell adherence was determined by an ex vivo binding assay. As controls, lymph nodes from mice that received footpad injections of either phosphate-buffered saline (PBS) alone or liposome-containing PBS were used. Use of macrophage- and neutrophil-specific monoclonal **antibodies** in tissue immunostaining showed that the L-**Cl2MDP** treatment eliminated macrophages but not neutrophils from the medullary and subcapsular sinus areas of the popliteal lymph nodes. A striking reduction of yeast cell adherence occurred with lymph nodes from L-Cl2MDP-treated mice compared with lymph nodes from control animals. The lymph node-yeast cell binding patterns of L-Cl2MDP-treated and control mice were the same regardless of mouse strain, sex, or T-cell competency. Results of India ink experiments, in which India ink was injected into footpads of mice and was rapidly taken up by popliteal lymph node macrophages, showed a strong correlation between yeast adherence and India ink staining of cells. In addition, the interaction of yeast cells with lymph node tissue from normal mice was not significantly affected by the addition of two extracellular matrix proteins, fibronectin and laminin, during the ex vivo adherence assay. These data indicate that medullary and subcapsular sinus lymph node macrophages express an adhesion system similar to that described for mouse splenic marginal zone macrophages.

L28 ANSWER 5 OF 5 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 91275790 MEDLINE
DOCUMENT NUMBER: 91275790 PubMed ID: 1647300
TITLE: Selective depletion of macrophages prevents pituitary-adrenal activation in response to subpyrogenic, but not to pyrogenic, doses of bacterial endotoxin in rats.
AUTHOR: Derijk R; Van Rooijen N; Tilders F J; Besedovsky H O; Del Rey A; Berkenbosch F
CORPORATE SOURCE: Department of Pharmacology, Medical Faculty, Free University, Amsterdam, The Netherlands.
SOURCE: ENDOCRINOLOGY, (1991 Jul) 129 (1) 330-8.

Journal code: EGZ; 0375040. ISSN: 0013-7227.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199107
ENTRY DATE: Entered STN: 19910818
Last Updated on STN: 19910818
Entered Medline: 19910730

AB The mechanisms by which bacterial endotoxin [lipopolysaccharide (LPS)] stimulates the hypothalamo-pituitary-adrenal axis (HPAA) have not been elucidated. The present study was designed to investigate the involvement of macrophages in plasma ACTH and corticosterone responses to LPS administration in rats using selective in vivo macrophage depletion. Intraperitoneal administration of subpyrogenic doses of LPS to normal rats resulted in elevated plasma ACTH and corticosterone concentrations, measured 2 h later. The response showed a remarkable steep dose relationship, with minimal effective doses between 0.5-1.5 micrograms (ACTH) and 0.5 micrograms or less (corticosterone)/kg BW. Plasma PRL, LH, and catecholamine (norepinephrine, epinephrine) levels were not significantly changed under the conditions used. Only at 6 h after LPS administration was a small elevation of norepinephrine noted. To deplete macrophages, rats were injected with liposomes encapsulated with dichloromethylene diphosphonate (**Cl2MDP**). Histochemical (acid phosphatase) and immunocytochemical techniques (monoclonal **antibodies** to rat macrophages coded ED1 and ED3) were applied to examine the efficiency of macrophage elimination by the Cl2MDP liposomes in cytospins of peritoneal exudates and in sections of the liver and spleen. Since cells of the macrophage lineage are considered to be the main source of IL-1 in the circulation, we also measured circulating levels of immunoreactive interleukin-1 beta (IL-1) concentrations in control and Cl2MDP liposome-treated rats by the use of a newly developed RIA. Reduced numbers of macrophages were seen in peritoneal lavages of Cl2MDP liposome-treated animals, whereas the morphological appearance and numbers of mast cells, granulocytes, and T-cells were unaffected. Similarly, macrophages were effectively eliminated in the spleen, mesenteric lymph nodes, and liver, as inferred from the reduction of macrophage staining in these organs. Plasma IL-1 concentrations could only be detected in response to a pyrogenic (2.5 mg/kg, iv) and not to a subpyrogenic (0.025 mg/kg, ip) dose of LPS. The increase in plasma IL-1 concentrations in response to the pyrogenic dose of LPS, reaching levels of 20-40 ng/ml in control rats, was blunted in animals treated with the Cl2MDP liposomes. Macrophage depletion by Cl2MDP liposomes did not affect either resting plasma corticosterone levels or the corticosterone response to ether exposure. At subpyrogenic doses of LPS, plasma ACTH and corticosterone responses were completely prevented by macrophage depletion. In contrast, at pyrogenic doses of LPS, plasma ACTH and corticosterone responses were not significantly affected by depleting macrophages. These data demonstrate that activation of the HPAA by a subpyrogenic dose of LPS is macrophage dependent. However, macrophage-independent mechanisms mediate activation of the HPAA in response to a pyrogenic dose of LPS.

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(FILE 'HOME' ENTERED AT 09:36:34 ON 05 APR 2002)

FILE 'MEDLINE, CAPLUS, EMBASE' ENTERED AT 09:36:54 ON 05 APR 2002

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L1            7 S FCGAMMAR1
L2           65 S FC (1N) GAMMA (1N) R1
L3         1957 S FC (1N) GAMMA (1N) RI
L4          982 S CD64
L5            0 S L1 AND L2 AND L3 AND L4
L6         2547 S L1 OR L2 OR L3 OR L4
L7         1130 S L6 (P) ANTIBOD?
L8           54 S L7 (P) ADMINIST?
L9           26 DUP REM L8 (28 DUPLICATES REMOVED)
L10         585 S VAN DE WINKEL?/AU
L11        1074 S L10 AND MACROPHAGE? OR CD64
L12         183 S L10 AND (MACROPHAGE? OR CD64)
L13         127 S L12 (P) ANTIBOD?
L14          11 S L13 (P) ADMINIST?
L15           7 DUP REM L14 (4 DUPLICATES REMOVED)
L16         299 S L4 (P) MACROPHAGE?
L17           0 S L16 AND PSORIASIS
L18          10 S L16 AND (HIV)
L19           5 DUP REM L18 (5 DUPLICATES REMOVED)
L20          23 S L16 AND (LUPUS OR SCLERODERMA OR DERMATITIS OR WEGENER? OR RA
L21          12 DUP REM L20 (11 DUPLICATES REMOVED)
L22         816 S (MAB (1N) 22) OR H22 OR (CRL (1N) 1117)
L23          58 S L22 (P) ADMINIST?
L24          35 DUP REM L23 (23 DUPLICATES REMOVED)
L25          33 S L24  NOT L7
L26         458 S CL2MDP
L27          10 S L26 (10N) ANTIBOD?
L28           5 DUP REM L27 (5 DUPLICATES REMOVED)
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=> end
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LOGOFF? (Y)/N/HOLD:y

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